Answer 1:

Bibliographic Information

Bcl-xL antisense oligonucleotide and cisplatin combination therapy extends survival in SCID mice with established mesothelioma xenografts. Littlejohn, James E.; Cao, Xiaobo; Miller, Steven D.; Ozvaran, Mustafa K.; Jupiter, Daniel; Zhang, Lidong; Rodarte, Charles; Smythe, W. Roy. Department of Molecular and Cellular Medicine, Texas A and M Health Science Center College of Medicine, College Station, TX, USA. International Journal of Cancer (2008), 123(1), 202-208. Publisher: Wiley-Liss, Inc., CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 149:167348 AN 2008:632471 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Bcl-xL functions as a dominant regulator of apoptotic cell death and is implicated in chemotherapeutic resistance of malignant pleural mesothelioma (MPM). Mesothelioma cell lines demonstrate increasing levels of Bcl-xL as resistant clones are selected in vitro. Moreover, upon introduction of antisense oligonucleotides specific to Bcl-xL mRNA, MPM cells are sensitized to chemotherapeutic agents. Here we describe the therapeutic effects of a novel combination therapy, Bcl-xL antisense oligonucleotide (ASO 15999) and cisplatin, on mesothelioma cell lines in vitro and in vivo; in addn., efficacy of ASO 15999 in decreasing tumor load as well as its effect on survival in an animal model. Finally, we initiated preliminary toxicity studies involved with i.p. (IP) injections of ASO 15999 into mice. This novel combination, with doses of cisplatin four times below established IC50 levels, significantly decreased viability of MPM cell lines after 48 h. The growth of established mouse flank human tumor xenografts was reduced with intra-tumor administration of ASO 15999. Local spread and development of IP xenografts was reduced with treatments of ASO alone, and survival of mice afflicted with these xenografts was prolonged after administration of ASO alone and ASO 15999 + cisplatin combination therapy. These findings suggest that ASO 15999 sensitizes MPM cell lines to the toxic effects of cisplatin. ASO 15999 induced redn. of Bcl-xL is effective in slowing the progression of human mesothelioma cell lines both in vitro and in vivo. More notably, the combination of Bcl-xL ASO and cisplatin extends survival in an orthotopic tumor xenograft model.

Answer 2:

Bibliographic Information

Response of preclinical medulloblastoma models to combination therapy with 13-cis retinoic acid and suberoylanilide hydroxamic acid (SAHA). Spiller, Susan E.; Ditzler, Sally H.; Pullar, Barbara J.; Olson, James M. Fred Hutchinson Cancer Research Center, Seattle, WA, USA. Journal of Neuro-Oncology (2008), 87(2), 133-141. Publisher: Springer, CODEN: JNODD2 ISSN: 0167-594X. Journal written in English. CAN 149:143382 AN 2008:623034 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Purpose: Current medulloblastoma therapy, surgery, radiation, and chemotherapy, is unacceptably toxic. However, 13-cis retinoic acid (RA) and SAHA, a histone deacetylase inhibitor, have each been shown to induce apoptosis in medulloblastoma cultures and mouse models. Both drugs cross the blood brain barrier, have been given safely to children, and achieve brain concns. that are at or near therapeutic levels. Retinoic acid acts by transcriptionally activating bone morphogenetic protein-2 (BMP-2) and SAHA facilitates transcriptional activity through chromatin accessibility. We tested the hypothesis that these drugs additively induce BMP-2 transcription and apoptosis. Exptl. design RA + SAHA induction of BMP-2 transcription and apoptosis in medulloblastoma cultures was evaluated. Subsequently the response of mouse medulloblastomas to these two agents in the presence and absence of cisplatin was evaluated. Results: BMP-2 transcription multiplied 3-fold with addn. of RA to culture, and 7-fold with both agents. The IC50 of SAHA was reduced by 40% when low dose RA was added. Interestingly, a p38 MAP kinase inhibitor that partially blocks RA-induced apoptosis did not inhibit the activity of RA + SAHA. Flank D283 tumors in athymic mice had slower growth in the RA + SAHA arm than single drug or control arms. Intracranial tumors in ND2:SmoAl mice treated with RA + SAHA + cisplatin showed a 4-fold increase in apoptosis over controls, and a 2-fold increase over animals receiving only SAHA or RA + SAHA. Conclusions: RA + SAHA additively induce BMP-2 transcription and medulloblastoma apoptosis. The combination may act through a p38 MAPK independent mechanism. Efficacy increased with cisplatin, which has implications for clin. trial design.

Answer 3:

Bibliographic Information

Effect of CDDP and ATRA on growth of xenografts of OCM-1 in nude mouse. Zhang, Jian; Luo, Min; Wang, Xiaoli; Chen, Yan. Department of Ophthalmology, Shanghai Ninth People's Hospital, School of Medicine, Shanghai Jiaotong University, Shanghai, Peop. Rep. China. Yanke Yanjiu (2008), 26(2), 104-107. Publisher: Henan Institute of Ophthalmology, CODEN: YAYAFH ISSN: 1003-0808. Journal written in Chinese. CAN 149:95687 AN 2008:543222 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Uveal melanoma is the most common eye malignant tumor in adult, which has a high mortality rate and responds poorly to the existing chemotherapy. How to reverse drug resistance and improve the prognosis of patients has become an important research point. Therefore the expt. was to study the influence of cis- diamminedichloroplatinum (CDDP) and /or all-trans retinoic acid (ATRA) on growth of xenografts of choroidal malignant melanoma lines (OCM) in nude mouse. 5*107/mL of cell suspension from OMC-1 was subdermally injected in 20 male Balb/c nude mice to create human OCM-1 xenograft model. The model mice were randomly divided into 4 groups. 2 Mg/kg of CDDP, 20mg/kg of ATRA and combination of 2mg/kg CDDP and 13.44mg/kg ATRA was i.p. administrated after 2 wk of modeling for 4 wk in group A, B, C resp., and group D was as the blank control group. The size of tumor were measured before and after usage of CDDP or/and ATRA, and the histol. alteration of tumor and apoptosis was examd. under the light microscope and TUNEL technol. The inhibition rate of CDDP to tumor was 43.2%, and that of ATRA was 37.65%, and the inhibition rate of the group CDDP +ATRA was 65.94%. The q value is 1.02(1.153>q>0.85) calcd. by Jin's formula. The mass doubling time of group A was obviously longer than that of blank control ($P<0.05$). The mass doubling time of group B was longer than that of blank control but without significant difference ($P>0.05$). The mass doubling time of group C was obviously longer than that of blank control ($P<0.01$). Through the TUNEL testing, all the tumor tissues of group A, B and C showed different degree of pos. staining. The combination of CDDP and ATRA has the stronger inhibition on the growth of xenografts of OCM-1 in nude mice, and its main mechanism may be related to the induction of apoptosis of tumor cells.

Answer 4:

Bibliographic Information

Circulating endothelial cells as a therapeutic marker for thalidomide in combined therapy with chemotherapy drugs in a human prostate cancer model. Li, Haiqing; Raia, Valentina; Bertolini, Francesco; Price, Douglas K.; Figg, William D. Molecular Pharmacology Section, Medical Oncology Branch, Center for Cancer Research, National Cancer Institute, NIH, Bethesda, MD, USA. BJU International (2008), 101(7), 884-888. Publisher: Blackwell Publishing Ltd., CODEN: BJINFO ISSN: 1464-4096. Journal written in English. CAN 149:44576 AN 2008:537069 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

OBJECTIVE: To investigate how thalidomide confers its survival benefit in prostate cancer, by assessing its effect on circulating endothelial cells (CECs) and progenitors (CEPs) in a combined therapy of thalidomide and chemotherapy drugs in a human prostate cancer xenograft model, as in clin. trials patients treated with both thalidomide and docetaxel had a >50% decrease in prostate-specific antigen (PSA) levels and longer median overall survival than those treated with docetaxel monotherapy. MATERIALS AND METHODS: A human prostate cancer xenograft model was used to evaluate the effect of either thalidomide, docetaxel or a combination of the two drugs on circulating ECs. Drug treatment was continued for 17 days, and tumors were measured two or three times a week. Blood samples were taken at three different time points: before the treatments, 4 days and 17 days into the treatments, and CECs and CEPs were measured by flow cytometry anal. RESULTS: There was an increased level of apoptotic/dead CECs shortly after the i.v. injection of docetaxel, and the addn. of thalidomide further increased the apoptotic/dead CEC level, showing that thalidomide enhances the cytotoxicity of docetaxel against tumor vascular ECs. CONCLUSION: Thalidomide increased the apoptotic/dead CEC level and enhanced the cytotoxicity of docetaxel against tumor vascular ECs, confirming its antiangiogenic property in vivo in combined anticancer treatments. In addn., there was a correlation between the increased apoptotic/dead CEC levels early in the treatment and antitumor efficacy later, suggesting that the apoptotic/dead CEC level could be used as a marker, at an early stage, to predict tumor response to antiangiogenic therapies.

Answer 5:

Bibliographic Information

NCX-4040, a nitric oxide-releasing aspirin, sensitizes drug-resistant human ovarian xenograft tumors to cisplatin by depletion of cellular thiols. Bratasz, Anna; Selvendiran, Karuppaiyah; Wasowicz, Tomasz; Bobko, Andrey; Khramtsov, Valery V.; Ignarro, Louis J.; Kuppusamy, Periannan. Center for Biomedical EPR Spectroscopy and Imaging, Davis Heart and Lung Research Institute, Department of Internal Medicine, The Ohio State University, Columbus, OH, USA. Journal of Translational Medicine (2008), 6 No pp. given. Publisher: BioMed Central Ltd., CODEN: JTMOBV ISSN: 1479-5876. http://www.translational-medicine.com/content/pdf/1479-5876-6-9.pdf Journal; Online Computer File written in English. CAN 149:94954 AN 2008:533169 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Background: Ovarian carcinoma is the leading cause of mortality among gynecol. cancers in the world. The high mortality rate is assocd. with lack of early diagnosis and development of drug resistance. The antitumor efficacy and mechanism of NCX-4040, a nitric oxide-releasing aspirin deriv., against ovarian cancer is studied. Methods: NCX-4040, alone or in combination with cisplatin (cis-diamminedichloroplatinum, cDDP), was studied in cisplatin-sensitive (A2780 WT) and cisplatin-resistant (A2780 cDDP) cell lines as well as xenograft tumors grown in nude mice. ESR (EPR) was used for measurements of nitric oxide and redox state. Immunoblotting anal. of A2780 cDDP tumor xenografts from mice was used for mechanistic studies. Results: Cells treated with NCX-4040 (25 μM) showed a significant redn. of cell viability (A2780 WT, 34.9 ± 8.7%; A2780 cDDP, 41.7 ± 7.6%; $p < 0.05$). Further, NCX-4040 significantly enhanced the sensitivity of A2780 cDDP cells (cisplatin alone, 80.6 ± 11.8% vs. NCX-4040 + cisplatin, 26.4 ± 7.6%; $p < 0.01$) and xenograft tumors (cisplatin alone, 74.0 = 4.4% vs. NCX-4040 + cisplatin, 56.4 ± 7.8%; $p < 0.05$), to cisplatin treatment. EPR imaging of tissue redox and thiol measurements showed a 5.5-fold redn. ($p < 0.01$) of glutathione in NCX-4040-treated A2780 cDDP tumors when compared to untreated controls. Immunoblotting anal. of A2780 cDDP tumor xenografts from mice treated with NCX-4040 and cisplatin revealed significant downregulation of pEGFR (Tyr845 and Tyr992) and pSTAT3 (Tyr705 and Ser727) expression. Conclusion: The results suggested that NCX-4040 could resensitize drug-resistant ovarian cancer cells to cisplatin possibly by depletion of cellular thiols. Thus NCX-4040 appears to be a potential therapeutic agent for the treatment of human ovarian carcinoma and cisplatin-resistant malignancies.

Answer 6:

Bibliographic Information

Inhibition of Stat3 activity by YC-1 enhances chemo-sensitivity in hepatocellular carcinoma. Lau, Chi Keung; Yang, Zhen Fan; Lam, Shuk Pik; Lam, Chi Tat; Ngai, Patricia; Tam, Ka Ho; Poon, Ronnie Tung-Ping; Fan, Sheung Tat. Center for Cancer Research and Department of Surgery, The University of Hong Kong, Pokfulam, Hong Kong, Peop. Rep. China. Cancer Biology & Therapy (2007), 6(12), 1900-1907. Publisher: Landes Bioscience, CODEN: CBTAAO ISSN: 1538-4047. Journal written in English. CAN 149:24288 AN 2008:461061 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The present study investigated the effect of YC-1, a novel anti-cancer agent, on the chemo-sensitivity of hepatocellular carcinoma (HCC). YC-1 was administered with chemo-cytotoxic drug, cisplatin, both in vitro and in vivo. YC-1 alone downregulated the expression of phosphorylated form of signal transducers and activators of transcription 3 (P-Stat3[705]), a key mediator in chemo-resistance. When combined with cisplatin, YC-1 further promoted tumor cell apoptosis, decreased the expression of P-Stat3(705), Bcl-xL, CyclinD1 and survivin, and induced the cleavage of caspase 9 and PARP. Overexpression of Stat3 reversed YC-1 induced cell death. YC-1 inhibited Stat3 activity by enhancing the polyubiquitination of P-Stat3(705) induced by cisplatin. In the in vivo setting, YC-1 combined with cisplatin remarkably suppressed tumor growth in a HCC xenograft model, and this effect was also accompanied by YC-1 mediated downregulation of P-Stat3(705), Bcl-xL, Cyclin D1 and survivin, and induction of cleaved caspase 9 and PARP in the tumor tissues. In conclusion, the present study demonstrated a novel anti-cancer effect of YC-1 in enhancing chemo-sensitivity of HCC cells to cisplatin through a Stat3 dependent manner. This finding provides insight into design of a new therapeutic strategy to improve efficacy of chemotherapy in HCC patients.

Answer 7:

Bibliographic Information

Gefitinib cytotoxicity in non-small cell lung cancer cells is enhanced by low dose cisplatin due to ligand-independent EGFR autophosphorylation. Hosaka, Takamichi; Ohmori, Tohru; Ando, Koichi; Ishida, Hiroo; Kusumoto, Sojiro; Sugiyama, Tomohide; Shirai, Takao; Okuda, Kentaro; Hirose, Takashi; Ohnishi, Tsukasa; Horichi, Naoya; Inoue, Fumiko; Sauo, Nagahiro; Kuroki, Toshio; Nakadate, Toshio; Adachi, Mitsuru. First Department of Internal Medicine, Showa University School of Medicine, 1-5-8, Hatanodai, Shinagawa-ku, Tokyo, Japan. Showa University Journal of Medical Sciences (2007), 19(3), 155-164. Publisher: Showa Medical Association and Showa University, CODEN: SUMSEG ISSN: 0915-6380. Journal written in English. CAN 148:440466 AN 2008:247055 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Epidermal growth factor receptor (EGFR) is a transmembrane receptor tyrosine kinase overexpressed in non-small cell lung cancer (NSCLC) and many other solid tumors. EGFR is activated by specific ligands and various cell stresses, such as oxidative stress and UV irradn. The present study investigates the effect of ligand-independent EGFR activation on gefitinib mediated cytotoxicity using the NSCLC cell line, PC-9. The induction of EGFR autophosphorylation by non-cytotoxic levels of hydrogen peroxide (H2O2) and cisplatin (CDDP) is completely inhibited by 100 nM gefitinib. Pretreatment of cells with both H2O2 and CDDP enhances gefitinib cytotoxicity in vitro. The growth inhibitory effect of gefitinib was examd. in vivo using the xenografted severe combined immunodeficiency (SCID) mouse model. PC-9 cells were pretreated with/without a low dose of CDDP (1 μM) for 1h and injected s.c. into the right flank of SCID mice. Following the appearance of measurable tumors mice were treated by s.c. injection into the left flank with / without 10 mg / kg gefitinib for 4 days. Pretreatment with CDDP enhanced tumor growth by 20-30% compared to the control. Subsequent treatment with gefitinib resulted in disappearance of the tumor mass by day 10 in the CDDP-pretreated group and by day 16 in the control group. There was no reappearance of tumors in the CDDP-pretreated group. By comparison, tumors reappeared in the non-pretreated group by day 20 in 4/5 animals. These results suggest that chemotherapy may enhance tumor growth due to ligand-independent EGFR activation and that combination chemotherapy may result in enhanced sensitivity of tumors to the sequential administration of gefitinib.

Answer 8:

Bibliographic Information

Sodium Thiosulfate Administered Six Hours after Cisplatin Does Not Compromise Antineuroblastoma Activity. Harned, Theresa M.; Kalous, Ondrej; Neuwelt, Alexander; Loera, Jason; Ji, Lingyun; Iovine, Peter; Sposto, Richard; Neuwelt, Edward A.; Reynolds, C. Patrick. Developmental Therapeutics Program, USC-CHLA Institute for Pediatric Clinical Research and Division of Hematology-Oncology Department of Pediatrics, Keck School of Medicine, University of Southern California and Children's Hospital Los Angeles, Los Angeles, CA, USA. Clinical Cancer Research (2008), 14(2), 533-540. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 149:119469 AN 2008:106222 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

PURPOSE: We detd. if the potentially otoprotective agent sodium thiosulfate (STS) could be given 6 h after cisplatin without diminishing the antineuroblastoma activity of cisplatin in human neuroblastoma cell lines in vitro (including cisplatin-resistant cell lines) and in neuroblastoma xenografts in vivo. Exptl. Design: We detd. the antineuroblastoma activity of cisplatin with or without the addn. of STS at 0 or 6 h after cisplatin in six neuroblastoma cell lines, both in std. cell culture conditions (20% O2) and in physiol. hypoxia (2% O2). Drug cytotoxicity was measured using the DIMSCAN fluorescence/digital imaging microscopy assay. In vivo studies of cisplatin combined with STS used a human neuroblastoma s.c. xenograft model (SMS-SAN) in athymic nu/nu mice. RESULTS: A significant protection against cisplatin cytotoxicity was seen when the neuroblastoma cells were exposed to cisplatin directly combined with STS. However, when cisplatin was given first and STS exposure occurred 6 h later, no effect on cisplatin cytotoxicity was obsd. In a s.c. neuroblastoma xenograft model in nu/nu mice, mice receiving cisplatin alone or cisplatin + STS at 6 h had significantly better progression-free survival rates ($P < 0.03$) compared with controls or mice treated with cisplatin + STS concurrently. There was no

statistically significant difference in outcomes between mice treated with cisplatin alone and the group treated with cisplatin followed by STS 6 h later (P = 0.9). CONCLUSION: These preclin. data suggest that the use of STS 6 h after cisplatin for otoprotection is unlikely to compromise the antineuroblastoma activity of cisplatin.

Answer 9:

Bibliographic Information

The inhibitory role of wogonin on tumor growth and telomerase activity of human ovarian cancer SKOV3 cell line xenograft in nude mice. Wei, Danrong; Zhang, Hanying; Zhang, Wei; Li, Li; Huang, Xinxin. Affiliated Tumor Hospital, Guangxi Medical University, Nanning, Peop. Rep. China. Zhongguo Yaolixue Tongbao (2007), 23(4), 534-538. Publisher: Anhui Yike Daxue Linchuan Yaoli Yanjiuso, CODEN: ZYTOE8 ISSN: 1001-1978. Journal written in Chinese. AN 2008:33970 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Telomerase is highly expressed in most tumor cells, and it is an ideal target for cancer mol. targeting therapy. It has been proved that wogonin effectively inhibits telomerase activity and tumor cell growth in vitro. The study was to explore the inhibitory effect of wogonin on the growth of tumor and telomerase activity of implanted human ovarian cancer cell line SKOV3 in nude mice. Nude mice with implanted human ovarian cancer cells SKOV3 were randomly divided into five groups, viz. the high dose group of wogonin (600 mg·kg-1), low dose group of wogonin (300 mg·kg-1), normal control group, cisplatin therapy group (3 mg·kg-1), and combined therapy group (cisplatin plus wogonin). The wt. of nude mice and the vol. of tumor were regularly measured. DNA, RNA and protein were extd. from the tumor tissue. The length of telomere was examd. by Southern blot. The expression of telomerase hTERT gene was detected by RT-PCR. The telomerase activity was examd. by TRAP-PCR-silver staining. The wogonin significantly inhibit the growth of tumor when compared with control group. The inhibitory rate of high dose group and low dose group were 56.67% and 38.10% (P=0.019), resp. The inhibitory rate of cisplatin therapy group was 50.83% (P=0.004). The suppress rate of combined group reached 66.9% and higher than that of any single therapy (P=0.002). The length of telomere in different concn. groups of wogonin was the same as that in the control group. Wogonin inhibited the expression of telomerase gene hTERT and telomerase activity. The inhibition is related to the dose of wogonin. Wogonin suppresses the growth and telomerase activity of tumor. The inhibitory effect is related to the dose of wogonin. Combination of wogonin and cisplatin increase the inhibitory rate in nude mice tumor.

Answer 10:

Bibliographic Information

Effects of the licorice extract against tumor growth and cisplatin-induced toxicity in a mouse xenograft model of colon cancer. Lee, Chang Ki; Park, Kwang Kyun; Lim, Soon Sung; Park, Jung Han Yoon; Chung, Won Yoon. Department of Oral Biology, Oral Cancer Research Institute, Oral Science Research Institute and Brain Korea 21 Project, Yonsei University College of Dentistry, Yonsei University, Seoul, S. Korea. Biological & Pharmaceutical Bulletin (2007), 30(11), 2191-2195. Publisher: Pharmaceutical Society of Japan, CODEN: BPBLEO ISSN: 0918-6158. Journal written in English. CAN 148:92535 AN 2008:24480 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Cisplatin is one of the most effective chemotherapeutic agents and plays a major role in the treatment of a variety of human solid tumors. However, its toxicity limits the clin. use. Recently, the administration of antioxidants has been suggested to protect against cisplatin-induced nephrotoxicity. The present study was designed to est. the antitumor activity of the licorice ext. alone and in combination with cisplatin, and its protective potential against cisplatin-induced toxicity in a mouse xenograft model. The administration of the licorice ext. significantly inhibited tumor growth in BALB/C mice inoculated with CT-26 colon cancer cells. The combination of the licorice ext. and cisplatin diminished the therapeutic efficacy of cisplatin but promoted considerably antitumor activity of the licorice ext. In mice with cisplatin treatment for 15 d, the serum levels of blood urea nitrogen and creatinine remarkably were increased by kidney damage, and the serum alanine aminotransferase and aspartate aminotransferase levels were elevated by liver damage.

The administration of the licorice ext. plus cisplatin recovered these functional indexes in the kidney and liver to almost the control levels. In addn., the administration of the licorice ext. significantly reduced the cisplatin-induced oxidative stress. Taken together, the administration of the licorice ext. inhibits the growth of mouse colon carcinoma without any adverse effects, and reduces the cisplatin-induced toxicity. Therefore, the licorice ext. may be a candidate for an anticancer and chemopreventive agent. However, cancer patients with cisplatin therapy should avoid the supplementation of the licorice ext.

Answer 11:

Bibliographic Information

Experimental study of antisense oligodeoxynucleotide targeting survivin gene for cisplatin resistant human lung adenocarcinoma xenograft in nude mice. Zhang, Meichun; Hu, Chengping; Chen, Qiong; Xia, Ying. Xiangya Hospital, Central South University, Changsha, Peop. Rep. China. Zhongnan Daxue Xuebao, Yixueban (2006), 31(5), 717-722. Publisher: Zhongnan Daxue Xuebao, Yixueban Bianjibu, CODEN: ZDXYCB ISSN: 1672-7347. Journal written in Chinese. CAN 148:322065 AN 2008:17955 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The feasibility of antisense oligodeoxynucleotide (ASODN) targeting survivin gene for cisplatin resistant human lung adeno-carcinoma xenograft in nude mice was explored. Cisplatin resistant cell lines A549/CDDP were cultured routinely with RPMI1640 medium. A549/CDDP cells were s.c. implanted in nude mice to establish cisplatin resistant xenograft animal models. After survivin ASODN mediated by cytofectin was directly injected into xenograft in 5 places. The vols. and wt. of tumor mass were detected, resp., and then tumor growth inhibitory rate and tumor growth index were calcd. The expression level of survivin mRNA and protein was detected by reverse transcription-polymerase chain reaction (RT-PCR) and immunochem. assay. In mice treated with single ASODN, the tumor growth inhibitory rate and tumor growth index was 35.4% and 4.23±0.4456. The difference of the tumor growth inhibitory rate and tumor growth index between blank control group and ASODN group was significant (P<0.05). While combined ASODN with cisplatin, the anticancer efficacy was far more significant and the tumor growth inhibitory rate was enhanced to 63.7%. The tumor growth index, however, reduced to 1.700±0.436, which was obviously significant, compared with the cisplatin group and other controls (P<0.05). The anticancer efficacy was even more obvious than that of ASODN group (P<0.05). Significant down-regulation of survivin mRNA and protein level expression in tumor tissues of ASODN group and ASODN and cisplatin group was detected by RT-PCR and immunochem. assay, resp. (P<0.05). Survivin ASODN mediated by cytofectin can inhibit the cisplatin resistant tumor growth by direct intra-tumoral injection. The anticancer efficacy may be assocd. with the down regulation of survivin expression. ASODN targeting survivin gene can be a supportive therapy to cisplatin resistant lung cancer, while the clin. effective values need further exploration.

Answer 12:

Bibliographic Information

Combining epigenetic and cytotoxic therapy in the treatment of solid tumors. Plimack, Elizabeth R.; Stewart, David J.; Issa, Jean-Pierre J. The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA. Journal of Clinical Oncology (2007), 25(29), 4519-4521. Publisher: American Society of Clinical Oncology, CODEN: JCONDN ISSN: 0732-183X. Journal; General Review written in English. CAN 148:134704 AN 2007:1282001 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A review. The research of Appleton et al. (2007) entitled "Phase I and pharmacodynamic trial of the DNA methyltransferase inhibitor decitabine and carboplatin in solid tumors" is reviewed with commentary and refs. Appleton et al. conducted trial combining decitabine and carboplatin in advanced solid tumors. This dose-finding trial uses a series of doses of decitabine that, per cycle, all fall within the range of low doses shown to induce hypomethylation in vitro and in vivo. Furthermore, decitabine was administered 8 days before initiation of cytotoxic therapy, in keeping with preclin. models. The investigators conducted two sep. dose escalations of decitabine, the first with carboplatin fixed at area under the concn. time curve (AUC) 5 and the second at AUC 6, concluding that the

recommended phase II dosing for this combination is decitabine 90 mg/rn2 administered on day 1 followed by carboplatin AUC 6 on day 8 of a 28-day cycle. Of the 30 patients assessable for response, one patient with melanoma had a partial response and three other patients had stable disease. The majority of responses clustered at the recommended combination dose.

Answer 13:

Bibliographic Information

The effects of various chemotherapy regimens on the expression of PCNA and Bcl-2 in human breast cancer xenograft (MCF-7) transplanted in nude mice. Wang, Yu-dong; Liu, Wei; Ji, Zhi-min; Zhang, Zhi-gang; Lv, Ya-lei; Wang, Shu-qin. Department of Medical Oncology, The 4th Hospital of Hebei Medical University, Shijiazhuang, Peop. Rep. China. Linchuang Zhongliuxue Zazhi (2007), 12(3), 173-176. Publisher: Institution of Chinese Clinical Oncology Journal, CODEN: LZZIA5 ISSN: 1009-0460. Journal written in Chinese. CAN 148:205626 AN 2007:1152600 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The objective of the paper is to investigate the effects of various chemotherapy regimens on the expression of PCNA and Bcl-2 of breast cancer, to assess the relationships between chemotherapy and two markers, and to evaluate the value of them to predict the response of chemotherapy. Forty-eight nude mice models of human breast cancer xenograft (MCF-7) were established, and then were randomly divided into control and 5 chemotherapy groups (each group, n = 8). Among 5 chemotherapy groups, mice were treated i.p. or orally by 5 chemotherapy regimens (CMF, CAF, NP, TP, Xeloda) resp. at two-thirds LD10 (dose lethal to 10% of the mice). Control animals were administered i.p. with normal saline. The pathol. feature of transplanted tumor was studied by HE stain, and the expression of Bcl-2 and PCNA was studied by SP immunohistochem. method. The expression of PCNA in 5 chemotherapy group was significantly lower than that of control (P<0.05), and the expression of PCNA in NP, TP and Xeloda groups was significantly lower than that of CMF and CAF groups (P<0.05). Moreover, the expression of PCNA was significantly correlated with pathol. therapeutic response (P=0.001). The expression of Bcl-2 in CAF, NP, TP, Xeloda groups was significantly higher than that of control (P<0.05). Moreover, the expression of Bcl-2 in TP group was significantly higher than that of CMF and CAF groups (P<0.05). The expression of Bcl-2 was not significantly correlated with the pathol. therapeutic response (P=0.093). Chemotherapy can increase the expression of PCNA, and decrease the expression of Bcl-2. Different chemotherapy regimens have different effects on PCNA and Bcl-2. PCNA can become a factor to evaluate the response to chemotherapy, and become possibly the prospective factor of chemoselect.

Answer 14:

Bibliographic Information

Inhibitory effect of recombinant human interleukin-24 on human gastric cancer xenografts in nude mouse. Yan, Su; Yang, Ji-cheng; Han, Mei; Zhao, Xiao-yu; Sheng, Wei-hua; Chen, Wei-chang. Affiliated First Hospital, Soochow University, Suzhou, Peop. Rep. China. Zhonghua Xiaohua Zazhi (2007), 27(8), 555-556. Publisher: Zhonghua Yixuehui, Shanghai Fenhui, CODEN: ZXZHC8 ISSN: 0254-1432. Journal written in Chinese. CAN 148:119718 AN 2007:1107741 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Interleukin (IL)-24 has inhibitory effect on the growth of multiple human tumor cells. It may induce apoptosis of tumor cells, suppress tumor cell growth and angiogenesis, without impact on normal cells, and inhibit the growth of human cancer xenografts in nude mice. The eukaryotic expression vector pcDNA3.0-IL-24 and the prokaryotic expression vector PET21a(+)IL-24 were successfully constructed by the department of cellular and mol. biol., medical college of Soochow University, which were stably expressed in Chinese hamster ovary (CHO) cells and E. coli BL21. On the basis of above research, recombinant human IL-24 (rhIL-24) protein, the expression product of the two plasmids was injected directly into the human gastric cancer s.c. xenografts in nude mice and the effect on the growth of gastric cancer xenografts in nude mice were obsd., in order to investigate the possible mechanism initially.

Answer 15:

Bibliographic Information

The combination of chemotherapy and intraperitoneal MegaFas Ligand improves treatment of ovarian carcinoma. Etter, Anne-Lise; Bassi, Isabelle; Germain, Stephane; Delaloye, Jean-Francois; Tschopp, Juerg; Sordat, Bernard; Dupuis, Marc. Preclinical Oncology, Apoxis SA, Lausanne, Switz. Gynecologic Oncology (2007), 107(1), 14-21. Publisher: Elsevier, CODEN: GYNOA3 ISSN: 0090-8258. Journal written in English. CAN 148:205507 AN 2007:1104694 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Objective: MegaFas Ligand (MFL) is a recombinant mol. that efficiently triggers apoptosis after binding to the Fas receptor expressed on target cells. The purpose of this study was to det. the potency of MFL in vitro and efficacy in vivo for i.p. treatment of mice implanted with human ovarian carcinoma cells. Methods: The potency of MFL was compared to that of other Fas agonists in a cytotoxicity assay on SKOV-3 cells. The potency of MFL was further detd. by measuring apoptosis in combination with cisplatin. The efficacy of MFL was detd. in vivo using peritoneal xenograft models of human ovarian carcinoma. Results: In vitro, MFL induced significantly higher levels of apoptosis than other Fas agonists, and was able to overcome the resistance of the ovarian cancer cell line SKOV-3 to Fas agonist antibody. MFL exerted an enhanced cytotoxic effect when combined with platinum-based drugs, leading to significantly more apoptosis than by incubation with MFL or these drugs alone. Treatment of mice xenografted with SKOV-3 and HOC79 ovarian tumors by i.p. administration of MFL alone or in combination with cisplatin resulted in a significant decrease in peritoneal tumor nodules and ascitic cells, and prolongation of survival as compared to non-treated mice. The beneficial effects of MFL treatment occurred in the absence of severe toxicity. Conclusion. MFL is a novel pro-apoptotic mol. that is able to efficiently induce apoptosis in ovarian cancer cells as well as to potentiate the activity of chemotherapeutic agents in vitro and in vivo.

Answer 16:

Bibliographic Information

Clinical and mechanistic aspects of glucocorticoid-induced chemotherapy resistance in the majority of solid tumors. Zhang, Chengwen; Wenger, Till; Mattern, Juergen; Ilea, Septimia; Frey, Christian; Gutwein, Paul; Altevogt, Peter; Bodenmueller, Wolfram; Gassler, Nikolaus; Schnabel, Philipp A.; Dienemann, Hendrik; Marme, Alexander; Hohenfellner, Markus; Haferkamp, Axel; Pfitzenmaier, Jesco; Groene, Hermann-Josef; Kolb, Armin; Buechler, Peter; Buechler, Markus W.; Friess, Helmut; Rittgen, Werner; Edler, Lutz; Debatin, Klaus-Michael; Krammer, Peter H.; Rutz, Hans P.; Herr, Ingrid. Research Group Molecular OncoSurgery, University of Heidelberg, Heidelberg, Germany. Cancer Biology & Therapy (2007), 6(2), 278-287. Publisher: Landes Bioscience, CODEN: CBTAAO ISSN: 1538-4047. Journal written in English. CAN 147:479951 AN 2007:1039338 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Glucocorticoids have been used widely in conjunction with cancer therapy due to their ability to induce apoptosis in hematol. cells and to prevent nausea and emesis. However, recent data including ours, suggest induction of therapy-resistance by glucocorticoids in solid tumors, although it is unclear whether this happens only in few carcinomas or is a more common cell type specific phenomenon. We performed an overall statistical anal. of our new and recent data obtained with 157 tumor probes evaluated in vitro, ex vivo and in vivo. The effect of glucocorticoids on apoptosis, viability and cell cycle progression under diverse clin. important questions was examd. New in vivo results demonstrate glucocorticoid-induced chemotherapy resistance in xenografted prostate cancer. In an overall statistical anal. we found glucocorticoid-induced resistance in 89% of 157 analyzed tumor samples. Resistance is common for several cytotoxic treatments and for several glucocorticoid-derivs. and due to an inhibition of apoptosis, promotion of viability and cell cycle progression. Resistance occurred at clin. achievable peak plasma levels of patients under anti-emetic glucocorticoid therapy and below, lasted for a long time, after one single dose, but was reversible upon removal of glucocorticoids. Two nonsteroidal alternative anti-emetic agents did not counteract anticancer treatment and may be sufficient to replace glucocorticoids in cotreatment of carcinoma patients. These data demonstrate the need for prospective clin. studies as well as for detailed mechanistic studies of GC-induced cell-type specific pro- and anti-apoptotic signaling.

Answer 17:

Bibliographic Information

Bcl2/bcl-xL inhibitor engenders apoptosis and increases chemosensitivity in mesothelioma. Cao, Xiaobo; Rodarte, Charles; Zhang, Lidong; Morgan, Clinton D.; Littlejohn, James; Smythe, W. Roy. Section of Surgery Research, Department of Surgery, Scott & White Memorial Hospital and Clinic; Scott, Sherwood and Brindley Foundation; Health Science Center, College of Medicine, The Texas A and M University System, Temple, TX, USA. Cancer Biology & Therapy (2007), 6(2), 246-252. Publisher: Landes Bioscience, CODEN: CBTAAO ISSN: 1538-4047. Journal written in English. CAN 147:496071 AN 2007:1039332 CAPLUS

Abstract

Meosthelioma is a neoplasm of the pleura that is currently incurable by conventional therapies. Previously, we demonstrated that mesothelioma overexpresses BCL-XL, an anti-apoptotic member of the BCL-2 family. In addn., we have shown that downregulation of BCL-XL using a BCL-XL antisense oligonucleotide engenders mesothelioma apoptotic cell death in vitro and in vivo. The purpose of this study is to evaluate the efficacy of bcl2/bcl-xL inhibitor, 2-methoxy antimycin A3, in inducing apoptosis and increasing chemo-sensitivity in vitro and in vivo. Several bcl-xL high-expression tumor cell lines and one normal human cell line were exposed to 2-methoxy antimycin A3. 2-Methoxy antimycin A3 demonstrated significantly growth inhibition only in these tumor cell lines, with little effect on normal human cells. Treatment with 2-methoxy antimycin A3 alone resulted in a dramatic increase in the induction of apoptosis in the cancer cells. Apoptosis occurs through decreasing mitochondrial membrane potential and caspase activation. Notably, treatment with 2-methoxy antimycin A3 does not alter BCL-2 family protein expression. Synergistic inhibition of tumor growth by the coadministration of cisplatin and 2-methoxy antimycin A3 was obsd. in both in vitro and in vivo expts. Together, these findings indicate that exposure of cancer cells to small mol. Bcl-2/xL inhibitors such as 2-methoxy antimycin A3 alone, or in the combination with other chemotherapeutics, may represent a novel therapeutic strategy in treatment of cancer, esp. mesothelioma.

Answer 18:

Bibliographic Information

Effects of Suramin in combination with cisplatin on growth and metastasis of lung adenocarcinoma xenografts in mice. Zhang, Ping; He, Jianbin; Ou, Liwen; Wang, Xiaohua. The First Affiliated Hospital, Nanhua University, Hengyang, Hunan Province, Peop. Rep. China. Aizheng (2006), 25(4), 409-413. Publisher: Sun Yat-sen Daxue, Aizheng Zhongxin, CODEN: AIZHE4 ISSN: 1000-467X. Journal written in Chinese. CAN 148:182558 AN 2007:949637 CAPLUS

Abstract

This study was to explore inhibitory effects of angiogenesis inhibitor Suramin in combination with cisplatin (DDP) on growth and lung metastasis of lung adenocarcinoma LA795 cell xenografts in mice. Highly metastatic LA795 cells were inoculated into mammary fatty pad of 32 T739 mice to establish lung adenocarcinoma models. Four days after inoculation, the mice were randomized into 4 groups: the mice in control group received i.p. injection of 0.2 mL normal saline everyday, the mice in DDP group received injection of DDP [2 mg/(kg/day)-1] at the 4th, 11th and 18th days, the mice in Suramin group received injection of Suramin [10 mg/(kg/day)-1] everyday, and the mice in combination group received injection of DDP [2 mg/(kg/day)-1] at the 4th, 11th, and 18th days and Suramin [10 mg/(kg/day)-1] everyday. All the mice were killed 24 days later. Lung and s.c. tumors were examd. histol. The metastatic tumor foci on lung surface were obsd., lung wt. was measured, the occurrence rate of lung metastasis and the inhibitory rate of metastatic foci were calcd., s.c. tumor microvessel d. (MVD), vascular endothelial growth factor (VEGF) and nuclear factor-κB (NF-κB) were detd. by immunohistochem., and tumor cell apoptosis was measured by TUNEL method. In the DDP, Suramin and combination groups, tumor growth was suppressed significantly, with growth inhibitory rates of 23.0%, 34.4% and 56.3%, resp. ($P<0.05$). Necrosis and decrease of tumor vessels were obsd. in the Suramin and combination groups. The expression of NF-κB was significantly lower, and tumor cell apoptosis index was significantly higher in the DDP, Suramin and combination groups than in the control group ($P<0.01$). The metastatic foci on lung surface were less in the Suramin and combination groups than in the DDP and control groups. The expression of MVD and VEGF in s.c. tumors and the occurrence rate of lung metastasis were also obviously lower in the Suramin and combination groups.

Suramin has synergetic inhibitory effect with DDP on growth and metastasis of lung adenocarcinoma LA795 cell xenografts in mice through inhibiting angiogenesis and inducing cell apoptosis.

Answer 19:

Bibliographic Information

Predicting the active doses in humans from animal studies: a novel approach in oncology. Rocchetti, M.; Simeoni, M.; Pesenti, E.; De Nicolao, G.; Poggesi, I. Preclinical Development, Nerviano Medical Sciences, Nerviano, Italy. European Journal of Cancer (2007), 43(12), 1862-1868. Publisher: Elsevier Ltd., CODEN: EJCAEL ISSN: 0959-8049. Journal written in English. CAN 147:461695 AN 2007:895461 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The success rate of clin. drug development is significantly lower in oncol. than in other therapeutic areas. Predicting the activity of new compds. in humans from preclin. data could substantially reduce the no. of failures. A novel approach for predicting the expected active doses in humans from the first animal studies is presented here. The method relies upon a PK/PD model of tumor growth inhibition in xenografts, which provides parameters describing the potency of the tested compds. Anticancer drugs, currently used in the clinic, were evaluated in xenograft models and their potency parameters were estd. A good correlation was obtained between these parameters and the exposures sustained at the therapeutically relevant dosing regimens. Based on the corresponding regression equation and the potency parameters estd. in the first preclin. studies, the therapeutically active concns. of new compds. can be estd. An early knowledge of level of exposure or doses to be reached in humans will improve the risk evaluation and decision making processes in anticancer drug development.

Answer 20:

Bibliographic Information

Effect on xenograft of nude mouse by combination therapy of nm23-h1 and cisplatin loaded albumin. Zhi, Keqian; Chen, Weihui; Wen, Yuming. Stomatology Hospital, Xian Jiaotong University, Xian, Shanxi Province, Peop. Rep. China. Huaxi Kouqiang Yixue Zazhi (2006), 24(2), 170-172. Publisher: Huaxi Kouqiang Yixue Zazhi Bianjibu, CODEN: HKYZA4 ISSN: 1000-1182. Journal written in Chinese. CAN 147:203212 AN 2007:790947 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effects of cisplatin loaded albumin and nm23-H1 therapy on the tumor of nude mouse were studied. The 15 BALB/C female mice were divided into three groups, the control group, cisplatin loaded albumin group and cisplatin loaded albumin plus nm23-H1 plasmid group. Tca8113 were injected into the mice s.c. with the concn. of 3.1×106 cells/mL. After two weeks, the mixt. of lipofectin and nm23-H1 was injected around xenograft of nude mouse. After three days, cisplatin loaded albumin was injected around xenograft. The wt. of mouse and the vol. and the wt. of xenograft were measured. The wt. of mouse was the lightest in the control group. The vol. and wt. of the transplanted tumor were the lightest in cisplatin loaded albumin plus nm23-H1 plasmid group. The tumor inhibition rates in cisplatin loaded albumin group and cisplatin loaded albumin plus nm23-H1 plasmid group were 15.8% and 49.5%, resp. The combination therapy of nm23-H1 and cisplatin loaded albumin could effectively inhibit the growth of xenograft in nude mouse.

Answer 21:

Bibliographic Information

The essential role of the mitochondria and reactive oxygen species in cisplatin-mediated enhancement of Fas ligand-induced apoptosis in malignant pleural mesothelioma. Stewart, John H.; Tran, Thai-Lan; Levi, Nicole; Tsai, Wilson S.; Schrump, David S.; Nguyen, Dao M. Department of Surgery, Wake Forest University School of Medicine, Winston-Salem, NC,

USA. Journal of Surgical Research (2007), 141(1), 120-131. Publisher: Elsevier, CODEN: JSGRA2 ISSN: 0022-4804. Journal written in English. CAN 147:377839 AN 2007:654853 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Cytotoxic chemotherapeutic drugs such as cisplatin (CDDP) synergistically interact with sol. Fas ligand (sFasL) to mediate profound induction of apoptosis in cancer cells, particularly those refractory to this death-inducing ligand. The goal of this study was to evaluate the roles of the mitochondria-dependent apoptotic cascade and the CDDP-generated reactive oxygen species (ROS) in mediating the supra-additive enhancement of cytotoxicity and apoptosis in combination-treated malignant pleural mesothelioma (MPM) cells. MPM cells were treated with sequential CDDP/sFasL in vitro. Cell viability and apoptosis were detd. by MTT and terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling assays. Stable transfectants expressing high levels of Bcl2 were created by retroviral gene transfer. Specific proteolytic activity of caspases 3, 8, and 9 were measured using fluorescent substrates. Pretreating MPM cells with CDDP increased their susceptibility to sFasL by 2- to more than 20-fold. Overexpression of either Bcl-2, the selective caspase 9 inhibitor z-LEHD-fmk, or the antioxidant N-acetylcysteine significantly abrogated combination-induced cytotoxicity and apoptosis. Moreover, the robust activation of caspase 8 in combination-treated cells was completely suppressed by Bcl-2 overexpression, thus implicating a mitochondria-mediated amplification feedback loop. As an in vivo correlate, sequential i.p. administration of CDDP and sFasL significantly inhibited the growth of i.p. MPM human xenografts in nude mice. The data indicate that the mitochondria-dependent feedback loop of the caspase activation cascade and the generation of ROS are both essential in mediating profound cytotoxicity and apoptosis of MPM cells treated with CDDP and sFasL. This mechanistic study establishes a the translational framework for the clin. application of sequential CDDP/sFasL in the treatment of MPM.

Answer 22:

Bibliographic Information

Combined effects of soluble vascular endothelial growth factor receptor FLT-1 gene therapy and cisplatin chemotherapy in human tongue carcinoma xenografts. Gao, Zhen-Nan; Wei, Yu-Quan; Yang, Pi-Shan; Xu, Xin; Zhao, Hua-Qiang; Huan, Xin; Kang, Bing. State Key Laboratory of Biotherapy, Sichuan University, Chengdu City, Peop. Rep. China. Oral Oncology (2007), 43(5), 477-483. Publisher: Elsevier Ltd., CODEN: EJCCER ISSN: 1368-8375. Journal written in English. CAN 147:180767 AN 2007:419614 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The aim of the present study was to assess the anti-tumor effect of a defective adenovirus that expresses sol. vascular endothelial growth factor (VEGF) receptor FLT-1 (AdsFLT-1) in combination with cisplatin (cis-diamminedichloroplatinum, DDP) on human tongue carcinoma Tca8113 cell xenografts that had been pre-established in nude mice. In vitro, Tca8113 cells secreted sol. FLT-1 (sFLT-1) after infection with AdsFLT-1, and the conditioned medium from AdsFLT-1-treated Tca8113 cells seemed to inhibit VEGF-induced proliferation of human umbilical vein endothelial cells. The combined effects of sFLT-1 gene therapy and DDP chemotherapy was then studied in well-established Tca8113 xenografts. The concn. of sFLT-1 in serum reached a peak 8 days after intratumoral injection of AdsFLT-1. In these tumors, AdsFLT-1 intratumoral injections had only a small effect. Interestingly, when the cells were also exposed to DDP chemotherapy, significantly higher ($P < 0.05$), and possibly synergistic, anti-tumoral effects were obsd. that were highly correlated to a marked redn. in intratumoral vascularization and an increase in tumor-cell apoptosis. Together, these data emphasize the potential of combining an anti-angiogenic gene therapy strategy with a destructive approach directed against the tumor cells to fight human tongue carcinoma.

Answer 23:

Bibliographic Information

Effects of various chemotherapy regimens on the expression of PCNA and growth of human breast cancer xenograft (MCF-7) in nude mice. Wang, Yu-dong; Liu, Wei; Ji, Zhi-min; Zhang, Zhi-gang; Wang, Jun-ling; Yan, Xia; Zhang, Xiang-hong. Department of Medical Oncology, 4th Hospital, Hebei Medical University, Shijiazhuang Hebei, Peop. Rep. China. Zhongguo Aizheng Zazhi

(2007), 17(2), 139-143. Publisher: Fudan Daxue Fushu Zhongliu Yiyuan, CODEN: ZAZHAF ISSN: 1007-3639. Journal written in Chinese. CAN 147:86596 AN 2007:395164 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Although standardized therapy has been widely adapted in clin. practice and results are being improved, effective protocols for truly individualized chemotherapy is still lacking. The anti-tumor activity of different combination regimens on human breast cancer xenograft (MCF-7) transplanted in nude mice and their impacts on the expression of PCNA were investigated, and to evaluate the value of PCNA as predictive factors for the res. 88 Nude mice with human breast cancer xenograft (MCF-7) were randomly divided into control and 10 chemotherapy groups, and 8 mice were assigned into each group. Among 5 chemotherapy groups, they were treated either i.p. or orally by 5 different combinations of chemotherapy regimens (CMF, CAF, NP, TP, Xeloda) at one-third of LD10 dosage, and another 5 chemotherapy groups were treated at two-third . Control animals were given normal saline i.p. The body wt. of nude mice and transplanted tumor growth were recorded on a regular basis, and tumor growth inhibition was calcd. The pathol. features of the transplanted tumor were studied under the microscope before and after treatment. The expression of PCNA was evaluated by SP immunohistochem. method and flow cytometry. The results show that body wt. and tumor wt. of nude mice treated by two-third LD10 dosage of various chemotherapy combinations were significantly lower than that in the control ($P<0.05$), and the inhibition rate of tumor growth for the groups we. The results showed that the two-third LD10 dosage of chemotherapy could reflect the anti-tumor effect of various combinations chemotherapy better and more accurately, so this dosage was used for the next study. The expression at PCNA by immunohistochem. studies shows that the expression of PCNA in every chemotherapy group was significantly lower than that of the control ($P<0.05$).

Moreover, the expressions of PCNA in NP group was significantly lower than that of CMF, CAF, TP and Xeloda group ($P<0.05$), while TP and Xeloda group was significantly lower than that of CMF and CAF group ($P<0.05$). FCM anal. shows that FI value of PCNA in every chemotherapy group was significantly lower than that of the control ($P<0.05$). FI value of PCNA in TP and Xeloda group was significantly lower than that of CMF and CAF group ($P<0.05$), while NP group a significantly lower than that of CMF group ($P<0.05$). Relationship between PCNA expression and pathol. response shows that the expression of PCNA was pos. correlated with pathol. therapeutic response of transplanted breast carcinoma ($r=0.540$, $P<0.05$). It was concluded that in vivo chemosensitivity testing with two third LD10 dosage of various combinations of chemotherapy cancer could somewhat predict the clin. situations. All of various chemotherapy regimens can decrease the expression of PCNA in breast cancer. The expression of PCNA could perhaps serve as the factor to judge the response to chemotherapy, and play a role in the selection of the kind of chemotherapy to be used in the clinic.

Answer 24:

Bibliographic Information

Antitumor efficacy of the cytotoxic RNase, ranpirnase, on A549 human lung cancer xenografts of nude mice. Lee, Intae; Kalota, Anna; Gewirtz, Alan M.; Shogen, Kuslima. Department of Radiology, University of Pennsylvania, Philadelphia, PA, USA. Anticancer Research (2007), 27(1A), 299-308. Publisher: International Institute of Anticancer Research, CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 147:157614 AN 2007:361431 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The cytotoxic RNase, ranpirnase (ONCONASE, ONC), may have promising therapeutic implication as an alternative for cisplatin for the treatment of lung cancer, due to inhibition of protein synthesis by t-RNA cleavage. A549 and NCI-H1975 human NSCLC cell lines were cultured in the presence and absence of ONC. Cytotoxicity was monitored using a clonogenic assay. Using an inverted phase and fluorescence microscope, we studied whether apoptosis was induced by ONC in gefitinib-induced apoptosis-resistant A549 tumor cells. The therapeutic effectiveness of ONC was studied via single and multiple administrations on A549 human non-small cell lung cancer (NSCLC), including tumors previously untreatable by cisplatin. ONC-induced changes in ATP levels were also monitored by non-localized phosphorus MR spectroscopy. ONC significantly inhibited the cell growth of A549 tumors. Apoptosis was significantly induced by ONC in a dose-dependent manner. In animal studies, multiple small doses of ONC were more effective than one large single dose for the inhibition of tumor growth with reduced side-effects, probably due to the normalization of leaky tumor vessels. ONC in combination with cisplatin significantly reduced tumor growth of A549 tumors. In large tumors, including those unsuccessfully treated with cisplatin, ONC showed inhibition of tumor growth, while a second treatment of cisplatin did not. During monitoring by

non-localized phosphorus MR spectroscopy, ATP levels decreased, likely due to ONC-induced inhibition of oxygen consumption (QO2). ONC significantly inhibited tumor growth of A549 NSCLC cells in both in vitro and in vivo studies. This investigation suggests important potential clin. uses of ONC for the treatment of NSCLC cancer patients.

Answer 25:

Bibliographic Information

FTY720 induced bcl-associated and fas-independent apoptosis in human renal cancer cells in vitro and significantly reduced in vivo tumor growth in mouse xenograft. Ubai, Takanobu; Azuma, Haruhito; Kotake, Yatsugu; Inamoto, Teruo; Takahara, Kiyoshi; Ito, Yuko; Kiyama, Satoshi; Sakamoto, Takeshi; Horie, Shigeo; Muto, Satoru; Takahara, Shiro; Otsuki, Yoshinori; Katsuoka, Yoji. Department of Urology, Osaka Medical College, Takatsuki, Osaka, Japan. Anticancer Research (2007), 27(1A), 75-88. Publisher: International Institute of Anticancer Research, CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 146:513990 AN 2007:361405 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A unique immunosuppressant, FTY720, selectively induces apoptosis in activated lymphocytes, but not in other hematopoietic cells. The potential that this unique mechanism could provide anticancer potential by inducing apoptosis in the human renal cancer cell line, ACHN, which is resistant to cisplatin, and its mol. pathway was investigated. The difference in drug susceptibility to FTY720 between cancer cells and non-cancer cells was examd. by MTT assay and flow cytometry. Apoptosis assay, including TUNEL staining, electron microscopy and DNA electrophoresis, was performed and the mol. pathway of FTY720 was evaluated by real time RT-PCR and Western blot. The in vivo effect of FTY720 was evaluated using a murine zenograft model. The susceptibility to FTY720 was significantly higher in ACHN cancer cells than in normal renal tubular cells (HK-2) at a concn. of less than 30 μM, while the susceptibility to cisplatin was even higher in HK-2 than in ACHN. Cancer cells treated with FTY720 showed findings typical of apoptosis with highly condensed nuclear chromatin and fragmented nuclei. The mol. anal. revealed that FTY720-induced apoptosis was mediated by a Fas-independent, Bcl-assocd. signal transduction pathway, and that inhibition of extracellular signal-regulated kinase (ERK) activity was involved in its underlying mechanism of action. FTY720 treatment significantly prevented in vivo tumor growth without any severe adverse reactions, while cisplatin treatment did not inhibit tumor growth despite exhibiting severe side-effects. FTY720 may be a promising candidate for a new anticancer therapy of renal cancer.

Answer 26:

Bibliographic Information

Tumor growth inhibition with cetuximab and chemotherapy in non-small cell lung cancer xenografts expressing wild-type and mutated epidermal growth factor receptor. Steiner, Philipp; Joynes, Christopher; Bassi, Rajiv; Wang, Su; Tonra, James R.; Hadari, Yaron R.; Hicklin, Daniel J. ImClone Systems Incorporated, New York, NY, USA. Clinical Cancer Research (2007), 13(5), 1540-1551. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 147:22955 AN 2007:230062 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Targeting the epidermal growth factor receptor (EGFR) is a validated approach to treat cancer. In non-small cell lung cancer (NSCLC), EGFR contains somatic mutations in 10% of patients, which correlates with increased response rates to small mol. inhibitors of EGFR. We analyzed the effects of the monoclonal IgG1 antibody Erbitux (cetuximab) in NSCLC xenografts with wild-type (wt) or mutated EGFR. NSCLC cell lines were grown s.c. in nude mice. Dose-dependent efficacy was established for cetuximab. To det. whether combination therapy produces tumor regressions, cetuximab was dosed at half-maximal efficacy with chemotherapy used at max. tolerated dose. Cetuximab showed antitumor activity in wt (A549, NCI-H358, NCI-H292) and mutated [HCC-827 (delE746-A750), NCI-H1975 (L858R, T790M)] EGFR-expressing xenografts. In the H292 model, cetuximab and docetaxel combination therapy was more potent to inhibit tumor growth than cetuximab or docetaxel alone. Cisplatin augmented efficacy of cetuximab to produce 6 of 10 regressions, whereas 1 of 10 regressions was found with cetuximab and no regression was found with cisplatin. Using H1975

xenografts, gemcitabine increased efficacy of cetuximab resulting in 12 of 12 regressions. Docetaxel with cetuximab was more efficacious with seven of nine regressions compared with single treatments. Cetuximab inhibited autophosphorylation of EGFR in both H292 and H1975 tumor lysates. Exploring the underlying mechanism for combination effects in the H1975 xenograft model, docetaxel in combination with cetuximab added to the antiproliferative effects of cetuximab but was the main component in this drug combination to induce apoptosis. Cetuximab showed antitumor activity in NSCLC models expressing wt and mutated EGFR. Combination treatments increased the efficacy of cetuximab, which may be important for the management of patients with chemorefractory NSCLC.

Answer 27:

Bibliographic Information

Suppression of colorectal tumor growth by regulated survivin targeting. Li, Binghua; Fan, Junkai; Liu, Xinran; Qi, Rong; Bo, Linan; Gu, Jinfa; Qian, Cheng; Liu, Xinyuan. Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, Peop. Rep. China. Journal of Molecular Medicine (Heidelberg, Germany) (2006), 84(12), 1077-1086. Publisher: Springer, CODEN: JMLME8 ISSN: 0946-2716. Journal written in English. CAN 146:287846 AN 2007:39660 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A major goal in cancer gene therapy is to develop efficient gene transfer protocols that allow tissue-specific and tightly regulated expression of therapeutic genes. The ideal vector should efficiently transduce cancer cells with minimal toxicity on normal tissues and persistently express foreign genes. One of the most promising regulatory systems is the mifepristone/RU486-regulated system, which has much lower basal transcriptional activity and high inducibility. In this work, we modified this system by incorporating a cancer-specific promoter, the human telomerase reverse transcriptase (hTERT) promoter. By utilizing hTERT promoter to control the regulator, RU486 could specifically induce the expression of foreign genes in cancer cells but not in normal cells. In the context of this system, a dominant neg. mutant of survivin (surDN) was controllably expressed in colorectal tumor cells. The surDN expression induced by RU486 showed a dosage- and time-dependent pattern. Regulated expression of surDN caused caspase-dependent apoptosis in colorectal tumor cells but had little effect on normal cells. Anal. of cell viability showed that RU486-induced expression of surDN suppressed colorectal tumor cell growth and had synergic effect in combination with chemotherapeutic agents. The potential of this system in cancer therapy was evaluated in exptl. animals. Tumor xenograft models were established in nude mice with colorectal tumor cells, and RU486 was i.p. administered. The results showed that conditional expression of surDN efficiently inhibited tumor growth in vivo and prolonged the life of tumor-burdened mice. Synergized with the chemotherapeutic drug cisplatin, regulated surDN expression completely suppressed tumor growth. These results indicated that this modified RU486-regulated system could be useful in cancer-targeting therapy.

Answer 28:

Bibliographic Information

Poly(γ,-glutamic acid)-cisplatin conjugate effectively inhibits human breast tumor xenografted in nude mice. Ye, Haifeng; Jin, Li; Hu, Rongzhang; Yi, Zhengfang; Li, Jing; Wu, Yelin; Xi, Xuguang; Wu, Zirong. Laboratory of Molecular Biology, School of Life Science, East China Normal University, Shanghai, Peop. Rep. China. Biomaterials (2006), 27(35), 5958-5965. Publisher: Elsevier Ltd., CODEN: BIMADU ISSN: 0142-9612. Journal written in English. CAN 146:12729 AN 2006:928056 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

An easily administered cis-dichlorodiammineplatinum (II) (CDDP) formulation with less toxicity and greater antitumor effect would be extremely valuable. We describe PGA-CDDP, a water-sol. CDDP deriv. The hydrolyzed γ-PGA has a mol. wt. between 45 and 60 kDa, and is a water-sol., biodegradable, and nontoxic polymer produced by microbial fermn. CDDP can be released from the resulting conjugate in PBS: there was initially a burst release during the first 6 h, followed by sustained release. In vitro, PGA-CDDP was less

potent than free CDDP at inhibiting cell growth in the Bcap-37 cell line. PGA-CDDP was given as 3 doses at an equiv. CDDP dose of 4 or 12 mg/kg with 2-day intervals between injections to Bcap-37-grafted mice. This treatment showed stronger antitumor activity and was less toxic than CDDP in vivo. Antitumor activity assays demonstrated that the PGA-CDDP conjugate treatment had significantly higher antitumor activity than control PBS treatment ($P < 0.01$). PGA-CDDP also increased the survival of mice bearing Bcap-37 cells with ref. to PBS treatment or free CDDP treatment. Furthermore, mice treated with PGA-CDDP (4 mg/kg, administered on day 0 and 5) showed no body wt. loss ($P > 0.05$ with respect to PBS treatment), whereas free CDDP treatment at the same dose caused a body wt. loss of 20-30% ($P < 0.001$). These findings suggest that PGA produced by microbial fermn. may be used as an effective drug carrier for CDDP and that PGA-CDDP may have potential applications in the treatment of human breast cancer.

Answer 29:

Bibliographic Information

Preclinical Characterization of AEG35156/GEM 640, a Second-Generation Antisense Oligonucleotide Targeting X-Linked Inhibitor of Apoptosis. LaCasse, Eric C.; Cherton-Horvat, Gabriele G.; Hewitt, Kimberley E.; Jerome, Lori J.; Morris, Stephen J.; Kandimalla, Ekambar R.; Yu, Dong; Wang, Hui; Wang, Wei; Zhang, Ruiwen; Agrawal, Sudhir; Gillard, John W.; Durkin, Jon P. Aegera Therapeutics, Inc., Montreal, QC, Can. Clinical Cancer Research (2006), 12(17), 5231-5241. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 146:454298 AN 2006:899348 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

PURPOSE: Cancer cells can use X-linked inhibitor of apoptosis (XIAP) to evade apoptotic cues, including chemotherapy. The antitumor potential of AEG35156, a novel second-generation antisense oligonucleotide directed toward XIAP, was assessed in human cancer models when given as a single agent and in combination with clin. relevant chemotherapeutics. Exptl. Design: AEG35156 was characterized for its ability to cause dose-dependent redns. of XIAP mRNA and protein in vitro and in vivo, to sensitize cancer cell lines to death stimuli, and to exhibit antitumor activity in multiple human cancer xenograft models as a single agent or in combination with chemotherapy. RESULTS: AEG35156 reduced XIAP mRNA levels with an EC50 of 8 to 32 nmol/L and decreased XIAP protein levels by >80%. Loss of XIAP protein correlated with increased sensitization to tumor necrosis factor-related apoptosis-inducing ligand (TRAIL)-mediated apoptosis in Panc-1 pancreatic carcinoma cells. AEG35156 exhibited potent antitumor activity relative to control oligonucleotides in three human cancer xenograft models (prostate, colon, and lung) and was capable of inducing complete tumor regression when combined with taxanes. Antitumor effects of AEG35156 correlated with suppression of tumor XIAP levels. CONCLUSIONS: AEG35156 reduces XIAP levels and sensitizes tumors to chemotherapy. AEG35156 is presently under clin. assessment in multiple phase I trials in cancer patients as a single agent and in combination with docetaxel in solid tumors or cytarabine/idarubicin in leukemia.

Answer 30:

Bibliographic Information

Antitumor efficacy of edotecarin as a single agent and in combination with chemotherapy agents in a xenograft model. Ciomei, Marina; Croci, Valter; Ciavolella, Antonella; Ballinari, Dario; Pesenti, Enrico. Department of Biology, Drug Discovery Oncology, Nerviano Medical Sciences, Milan, Italy. Clinical Cancer Research (2006), 12(9), 2856-2861. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 145:388833 AN 2006:532561 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The novel indolocarbazole edotecarin (J-107088, formerly ED-749) differs from other topoisomerase I inhibitors both pharmacokinetically and pharmacodynamically. In vitro, it is more potent than camptothecins and has a variable cytotoxic activity in 31 different human cancer cell lines. Edotecarin also possesses greater than additive inhibitory effects on cell proliferation when used in combination with other agents tested in vitro against various cancer cell lines. The present in vivo studies were done to extend the

in vitro findings to characterize the antitumor effects of edotecarin when used either alone or in combination with other agents (i.e., 5-fluorouracil, irinotecan, cisplatin, oxaliplatin, and SU11248) in the HCT-116 human colon cancer xenograft model. Treatment effects were based on the delay in onset of an exponential growth of tumors in drug-treated vs. vehicle control-treated groups. In all studies, edotecarin was active both as a single agent and in combination with other agents. Combination therapy resulted in greater than additive effects, the extent of which depended on the specific dosage regimen. Toxicity in these expts. was minimal. Of all 359 treated mice, the six that died of toxicity were in the high-dose edotecarin/oxaliplatin group. The results suggest that edotecarin may serve as effective chemotherapy of colon cancer when used as a single agent, in combination with std. regimens and other topoisomerase inhibitors or with novel agents, such as the multitargeted tyrosine kinase inhibitor SU11248.

Answer 31:

Bibliographic Information

p53 mutation and cyclin D1 amplification correlate with cisplatin sensitivity in xenografted human squamous cell carcinomas from head and neck. Henriksson, Eva; Baldetorp, Bo; Borg, Aake; Kjellen, Elisabeth; Aakervall, Jan; Wennerberg, Johan; Wahlberg, Peter. Department of Otorhinolaryngology, University Hospital of Malmoe, Malmoe, Swed. Acta Oncologica (2006), 45(3), 300-305. Publisher: Taylor & Francis Ltd., CODEN: ACTOEL ISSN: 0284-186X. Journal written in English. CAN 145:393563 AN 2006:408524 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

To investigate the response of tumor growth to cisplatin treatment, in relation to p53 mutation and cyclin D1 dysregulation on DNA and protein level, biopsies from seven xenografted human squamous cell carcinomas from the head and neck were analyzed with immunohistochem. for p53 expression and cyclin D1 expression. Polymerase chain reaction -singlestranded conformation polymorphism was used to det. p53 mutations. Fluorescence in situ hybridization was performed to analyze cyclin D1 amplification. The mice were injected i.p. with NaCl (controls) or cisplatin. After injection the tumor vol. were measured. The inhibition of tumor growth by cisplatin was defined as the area under the growth curves, and compared with the growth curves of the tumors in the control group. Xenografts with p53 mutation showed significantly higher resistance to cisplatin (p .apprx.0.001) and also tumors with cyclin D1 amplification showed significantly higher resistance (p .apprx.0.001).

Answer 32:

Bibliographic Information

Loss of Oct-3/4 Expression in Embryonal Carcinoma Cells Is Associated with Induction of Cisplatin Resistance. Mueller, Thomas; Mueller, Lutz Peter; Luetzkendorf, Jana; Voigt, Wieland; Simon, Heike; Schmoll, Hans-Joachim. Department of Medicine IV, Hematology/Oncology, Martin Luther University Halle-Wittenberg, Halle, Germany. Tumor Biology (2006), 27(2), 71-83. Publisher: S. Karger AG, CODEN: TUMBEA ISSN: 1010-4283. Journal written in English. CAN 145:327808 AN 2006:376764 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Although the majority of testicular germ cell tumors (TGCTs) are curable by cisplatin-based chemotherapy, in a few cases, the occurrence of cisplatin resistance results in a poor outcome. The biol. basis of this differential cisplatin sensitivity in TGCTs remains largely unexplained. Embryonal carcinoma (EC) cells represent the presumptive tumor stem cells in nonseminomatous TGCTs and are known to express the embryonal transcription factor Oct-3/4 and to be hypersensitive to cisplatin. In the present study, we analyzed TGCT cell lines and nude mouse xenografts showing differential cisplatin sensitivity. Here we demonstrate that a lack of expression of Oct-3/4 in TGCT cells is assocd. with a higher apoptotic threshold and cisplatin resistance which is accompanied by an impaired caspase-9 activation, reduced caspase-3 activity and altered p53 accumulation. We were able to induce loss of Oct-3/4 in a cisplatin-sensitive EC cell line resulting in a secondary cisplatin-resistant cell type with retained EC cell characteristics and changes in apoptotic signaling identical to those in primary resistant cells. Furthermore, we show that EC cells are retained in their undifferentiated state by Oct-3/4 and that a complete and ultimate loss of Oct-3/4 followed by an early differentiation step is necessary to establish

the cisplatin-resistant state. Our data suggest that loss of Oct-3/4 expression leads to induction of a higher apoptotic threshold and to cisplatin resistance in EC cells of nonseminomatous TGCTs. We hypothesize that in refractory TGCTs the original tumor stem cell population of Oct-3/4-pos., cisplatin-sensitive EC cells could be replaced by an Oct-3/4-neg., resistant population in a selection process. In contrast, the presence of the Oct-3/4-pos., highly sensitive EC cells as the tumor stem cell component in most TGCTs could explain the general high chemosensitivity and curability of these tumors.

Answer 33:

Bibliographic Information

Corticosteroid co-treatment induces resistance to chemotherapy in surgical resections, xenografts, and established cell lines of pancreatic cancer. Zhang, Chengwen; Kolb, Armin; Buechler, Peter; Cato, Andrew C. B.; Mattern, Juergen; Rittgen, Werner; Edler, Lutz; Debatin, Klaus-Michael; Buechler, Markus W.; Friess, Helmut; Herr, Ingrid. Research Group Molecular Urooncology, German Cancer Research Center, Heidelberg, Germany. BMC Cancer (2006), 6 No pp. given. Publisher: BioMed Central Ltd., CODEN: BCMACL ISSN: 1471-2407. http://www.biomedcentral.com/content/pdf/1471-2407-6-61.pdf Journal; Online Computer File written in English. CAN 144:425939 AN 2006:314605 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Background: Chemotherapy for pancreatic carcinoma often has severe side effects that limit its efficacy. The glucocorticoid (GC) dexamethasone (DEX) is frequently used as co-treatment to prevent side effects of chemotherapy such as nausea, for palliative purposes and to treat allergic reactions. While the potent pro-apoptotic properties and the supportive effects of GCs to tumor therapy in lymphoid cells are well studied, the impact of GCs to cytotoxic treatment of pancreatic carcinoma is unknown. Methods: A prospective study of DEX-mediated resistance was performed using a pancreatic carcinoma xenografted to nude mice, 20 surgical resections and 10 established pancreatic carcinoma cell lines. Anti-apoptotic signaling in response to DEX was examd. by Western blot anal. Results: In vitro, DEX inhibited drug-induced apoptosis and promoted the growth in all of 10 examd. malignant cells. Ex vivo, DEX used in physiol. concns. significantly prevented the cytotoxic effect of gemcitabine and cisplatin in 18 of 20 freshly isolated cell lines from resected pancreatic tumors. No correlation with age, gender, histol., TNM and induction of therapy resistance by DEX co-treatment could be detected. In vivo, DEX totally prevented cytotoxicity of chemotherapy to pancreatic carcinoma cells xenografted to nude mice. Mechanistically, DEX upregulated pro-survival factors and anti-apoptotic genes in established pancreatic carcinoma cells. Conclusions: These data show that DEX induces therapy resistance in pancreatic carcinoma cells and raise the question whether GC-mediated protection of tumor cells from cancer therapy may be dangerous for patients.

Answer 34:

Bibliographic Information

G3139 and Other CpG-Containing Immunostimulatory Phosphorothioate Oligodeoxynucleotides Are Potent Suppressors of the Growth of Human Tumor Xenografts in Nude Mice. Gekeler, Volker; Gimmnich, Petra; Hofmann, Hans-Peter; Grebe, Carola; Roemmele, Michaela; Leja, Astrid; Baudler, Monika; Benimetskaya, Luba; Gonser, Barbara; Pieles, Uwe; Maier, Thomas; Wagner, Thomas; Sanders, Karl; Beck, James F.; Hanauer, Guido; Stein, C. A. ALTANA Pharma AG, Konstanz, Germany. Oligonucleotides (2006), 16(1), 83-93. Publisher: Mary Ann Liebert, Inc., CODEN: OLIGAJ ISSN: 1545-4576. Journal written in English. CAN 145:116878 AN 2006:307685 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Several phosphorothioate antisense oligodeoxynucleotides (ODN) are developed to target factors potentially involved in tumor growth and apoptosis suppression. Among them, the 18-mer G3139 (Oblimersen), which targets Bcl-2, is currently being tested in phase II and phase III clin. trials for various tumors in combination with chemotherapy. On the other hand, ODNs contg. CpG dinucleotides (CpG-ODN) within specific-sequence contexts (CpG motifs) have been shown to activate rodent or primate immune cells via toll-like receptor 9 (TLR9) and have demonstrated remarkable T cell-dependent antitumor efficacy in a series of murine tumor models. However, immune cell activation by CpG-ODN is largely diminished upon C-5 methylation at CpG cytosine. As G3139 contains CpG

motifs, the authors questioned whether the antitumor effects seen in human tumor xenografts might be abrogated by cytosine C-5 methylation of G3139, which retained the ability of G3139 to suppress Bcl-2 expression in tissue culture, or by similar derivatization of other phosphorothioate ODNs developed for the immune activation of rodent or human cells. The in vivo antitumor efficacy of the immunostimulatory H1826 and H2006 ODNs was compared with that of G3139. Bcl-2 suppression achieved by G3139 purportedly sensitizes tumor cells toward cytotoxic agents, and some of the expts. employed combinations of ODN with such drugs as cisplatin or etoposide. H1826, H2006, and G3139 all produced similar, striking, growth inhibitory effects on either H69 SCLC, A2780 ovarian carcinoma, or A549 lung adenocarcinoma human tumor xenografts at doses of 0.3 mg/kg and 1 mg/kg (H1826, H2006) or 12 mg/kg (G3139) per day. In contrast, the H2006-mC (1 mg/kg) or G3139-mC (12 mg/kg) derivs. demonstrated no significant antitumor effects. The combination of G3139 (12 mg/kg) with cisplatin produced some additive antitumor efficacy, which was not seen in combinations of G3139-mC (12 mg/kg) or H1826 (1 mg/kg) with cisplatin.
G3139, at a dose of 12 mg/kg, alone induced extensive enlargement of the spleen. Immunostimulation was evaluated in vitro by flow cytometric measurements of the CD80 and CD86 activation markers found on CD19+ murine splenocytes. The CpG-ODN producing strong antitumor effects in vivo also induced these activation markers in vitro, in contrast to the in vivo inactive G3139-mC. Our data indicate a significant contribution of the immunostimulatory properties of CpG-ODN (including G3139) to the antitumor effects obsd. in nude mouse xenograft models. This is in contrast to previous data presented by other authors indicating that the activity of G3139 in human tumor xenografts was Bcl-2 specific. Furthermore, as nude mice are devoid of T cells, a T cell-mediated immune response apparently is not required for the potent antitumor responses obsd. here; innate immune responses are sufficient.

Answer 35:

Bibliographic Information

Glucocorticoid-mediated inhibition of chemotherapy in ovarian carcinomas. Zhang, Chengwen; Marme, Alexander; Wenger, Till; Gutwein, Paul; Edler, Lutz; Rittgen, Werner; Debatin, Klaus-Michael; Altevogt, Peter; Mattern, Juergen; Herr, Ingrid. Molecular Urooncology, German Cancer Research Center, Heidelberg, Germany. International Journal of Oncology (2006), 28(2), 551-558. Publisher: International Journal of Oncology, CODEN: IJONES ISSN: 1019-6439. Journal written in English. CAN 145:95902 AN 2006:150417 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The glucocorticoid dexamethasone is frequently used as a co-treatment in cytotoxic cancer therapy, e.g. to prevent nausea, to protect normal tissue or for other reasons. While the potent pro-apoptotic properties and supportive effects of glucocorticoids to tumor therapy in lymphoid cells are well studied, the impact on the cytotoxic treatment of ovarian carcinoma is unknown. We tested apoptosis-induction, viability, tumor growth and protein expression using established cell lines, primary cell lines freshly isolated from patient material and a xenograft on nude mice. We found a general induction of resistance toward cytotoxic therapy by DEX-co-treatment in most of the examd. ovarian cancer cells treated in vitro, ex vivo or in vivo. Resistance occurred independently of cell d. and was found at peak plasma levels of dexamethasone and below. Mechanistically, the dexamethasone-induced expression of survival genes may be involved in the resistance. These data show that glucocorticoid-induced resistance is common in ovarian carcinomas implicating that the use of glucocorticoids may be harmful for cancer patients.

Answer 36:

Bibliographic Information

Comparative anti-tumor efficacy of two orally administered platinum(IV) drugs in nude mice bearing human tumor xenografts. Sova, Petr; Mistr, Adolf; Kroutil, Ales; Zak, Frantisek; Pouckova, Pavla; Zadinova, Marie. Research and Development, PLIVA-Lachema a.s., Charles University, Prague, Czech Rep. Anti-Cancer Drugs (2006), 17(2), 201-206. Publisher: Lippincott Williams & Wilkins, CODEN: ANTDEV ISSN: 0959-4973. Journal written in English. CAN 144:324325 AN 2006:60669 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The oral anti-tumor activity of a novel platinum(IV) complex, coded as LA-12, with a bulky adamantylamine ligand was evaluated and compared with another platinum(IV) complex satraplatin. The human carcinoma xenografts of colon HCT116, prostate PC3, and ovarian A2780 and A2780/cisR (resistant to cisplatin) were used to evaluate the in-vivo anti-tumor activity. The daily×5 repeated dose regimen in equimolar doses of LA-12 and satraplatin, administered in 2 cycles, was selected for this evaluation. All doses of LA-12 and satraplatin were significantly effective in comparison with the control. The activities of LA-12 in all doses and all used tumor xenografts were higher than equimolar doses of satraplatin. The highest effect was reached with LA-12 at a dose of 60 mg/kg. The shapes of growth curves of ovarian carcinoma A2780 and its subline resistant to cisplatin after therapy with LA-12 were very similar. This shows that LA-12 is able to overcome resistance to cisplatin.

Answer 37:

Bibliographic Information

The modifier subunit of glutamate cysteine ligase relates to cisplatin resistance in human small cell lung cancer xenografts in vivo. Nishi, Masatake; Abe, Yoshiyuki; Fujimori, Sakashi; Hamamoto, Atsushi; Inoue, Yoshimasa; Miyazaki, Noriyuki; Oida, Yasuhisa; Ikoma, Norihiro; Ohnishi, Yasuyuki; Yamazaki, Hitoshi; Ueyama, Yoshito; Nakamura, Masato. Department of Pathology, Tokai University School of Medicine, Bohseidai, Isehara, Kanagawa, Japan. Oncology Reports (2005), 14(2), 421-424. Publisher: Oncology Reports, CODEN: OCRPEW ISSN: 1021-335X. Journal written in English. CAN 144:31990 AN 2005:778991 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Glutamate cysteine ligase (GCL) plays an important role in the intracellular detoxification of cisplatin (CDDP). GCL is composed of a modifier or light chain subunit (GCLM) and a catalytic or heavy chain subunit (GCLC). Previously, we showed that the GCL subunits enhanced CDDP-resistance in non-small cell lung cancer (NSCLC) xenografts. In small cell lung cancer (SCLC), it is unclear whether the GCL sub-units are essential to CDDP-resistance. We examd. the gene expression of GCLM and GCLC in four human SCLC xenografts with the real-time polymerase chain reaction (PCR). An in vivo drug sensitivity test with CDDP was performed on the SCLC xenografts. CDDP-resistance was examd. as the growth ratio of the relative vol. of the treated xenografts to the controls (T/C%). The expression level of GCLM gene in SCLC was significantly lower than that in NSCLC ($p=0.0026$, Welch's t-test). One of four SCLC xenografts showed 62% of T/C and this was evaluated as CDDP-resistance, while the other three xenografts were sensitive to CDDP in vivo (Mann-Whitney U-test, $p<0.01$, one-sided). The expression level of the GCLM gene was significantly correlated to T/C% (Fisher's test, $p=0.0289$, correlations = 0.975), while the GCLC gene expression level was not assocd. with T/C%. These results suggest that the overexpression of GCLM is correlated with CDDP-resistance in SCLC xenografts in vivo.

Answer 38:

Bibliographic Information

Combined effects of cantide and chemotherapeutic drugs on inhibition of tumor cells' growth in vitro and in vivo. Yang, Ying; Lv, Qiu-Jun; Du, Qing-You; Yang, Bing-Hu; Lin, Ru-Xian; Wang, Sheng-Qi. Beijing Institution of Radiation Medicine, Beijing, Peop. Rep. China. World Journal of Gastroenterology (2005), 11(16), 2491-2496. Publisher: World Journal of Gastroenterology, CODEN: WJGAF2 ISSN: 1007-9327. Journal written in English. CAN 143:109194 AN 2005:501149 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

AIM: To investigate the combination effect of hTERT antisense oligonucleotide "Cantide" and three chemotherapeutic drugs (cisplatin, 5-fluorouracil (5-FU) and adriamycin (ADM)) on inhibiting the proliferation of HepG2, BGC and A549 cell lines in vitro, and to investigate the efficacy of Cantide used in combination with cisplatin (DDP) in vivo. METHODS: Cantide was transfected into these tumor cells by Lipofectin, and cell growth activity was calcd. by microcytotoxicity assay. In vivo study, cells of HepG2 were implanted in Balb/c nude mice for 4 d. Then Cantide, DDP and Cantide+DDP were given i.p. for 24 d resp. The body wts. of the tumor-bearing animals and their tumor mass were measured later to assess the effect of combination therapy in the nude mice. To evaluate the interaction

of Cantide and these chemotherapeutic drugs, SAS software and Jin Zhengjun method were used. RESULTS: Combination treatments with 0.1 μmol/L Cantide reduced the IC50 of DDP, 5-FU and ADM from 1.07, 4.15 and 0.29 μg/mL to 0.25, 1.52 and 0.12 μg/mL resp. The inhibition ability of DDP, 5-FU and ADM resp. in combination with Cantide in these tumor cells was higher than that of these drugs alone ($P<0.0001$). And synergism ($Q \geq 1.15$) was obsd. at the lower concn. of DDP (≤ 1 μg/mL), 5-FU (≤10 μg/mL) and ADM (≤0.1 μg/mL) with combination of Cantide. In vivo, combination treatment with Cantide and DDP produced the greater growth inhibition of human liver carcinoma cells HepG2 in nude mice (0.65±0.19 g tumor) compared with that when only one of these drugs was used (Cantide group: 1.05±0.16 g tumor, $P = 0.0009<0.001$; DDP group: 1.13±0.09 g tumor, $P = 0.0001<0.001$). CONCLUSION: These findings indicate that Cantide may enhance therapeutic effectiveness of chemotherapeutic drugs over a wide range of tumor cells in vitro, and the combination use of Cantide and DDP can produce much higher inhibition rates, as compared with when either of these drugs was used only in vivo.

Answer 39:

Bibliographic Information

Circulating plasma vascular endothelial growth factor in mice bearing human ovarian carcinoma xenograft correlates with tumor progression and response to therapy. Manenti, Luigi; Riccardi, Elena; Marchini, Sergio; Naumova, Elitza; Floriani, Irene; Garofalo, Angela; Dossi, Romina; Marrazzo, Eleonora; Ribatti, Domenico; Scanziani, Eugenio; Bani, MariaRosa; Belotti, Dorina; Broggini, Massimo; Giavazzi, Raffaella. Laboratory of Biology and Therapy of Metastasis, Department of Oncology, Mario Negri Institute for Pharmacological Research, Bergamo, Italy. Molecular Cancer Therapeutics (2005), 4(5), 715-725. Publisher: American Association for Cancer Research, CODEN: MCTOCF ISSN: 1535-7163. Journal written in English. CAN 143:23937 AN 2005:418722 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Vascular endothelial growth factor (VEGF) performs as an angiogenic and permeability factor in ovarian cancer, and its overexpression was assocd. with poor prognosis. However, models to study its role as a marker of tumor progression are lacking. The authors generated xenograft variants derived from the A2780 human ovarian carcinoma (1A9), stably transfected with VEGF121 in sense (1A9-VS-1) and antisense orientation (1A9-VAS-3). 1A9, 1A9-VS-1, and 1A9-VAS-3 disseminated in the peritoneal cavity of nude mice, but only 1A9-VS-1, the VEGF121-overexpressing tumor variant, produced ascites. Tumor biopsies from 1A9-VS-1 showed alterations in the vascular pattern and caused an angiogenic response in the chorioallantoic membrane assay. A significant level of sol. VEGF was detectable in the plasma of mice bearing 1A9-VS-1 even at an early stage of tumor growth. Plasma VEGF correlated pos. with tumor burden in the peritoneal cavity and ascites accumulation. Cisplatin reduced the tumor burden and ascites in mice bearing 1A9-VS-1; the response was assocd. with a significant decrease of VEGF in plasma. This 1A9-VS-1 xenograft model reproduces the behavior of human ovarian cancer by growing in the peritoneal cavity, being highly malignant, and producing ascites. Plasma VEGF as a marker of tumor progression offers a valuable means of detecting early tumor response and following up treatments in an animal model.

Answer 40:

Bibliographic Information

Cisplatin represses transcriptional activity from the minimal promoter of the O6-methylguanine methyltransferase gene and increases sensitivity of human gallbladder cancer cells to 1-(4-amino-2-methyl-5-pyrimidinyl) methyl-3-2-chloroethyl)-3-nitrosourea. Sato, Ken; Kitajima, Yoshihiko; Nakagawachi, Tetsuji; Soejima, Hidenobu; Miyoshi, Atsushi; Koga, Yasuo; Miyazaki, Kohji. Department of Surgery, Department of Biomolecular Sciences, Saga University Faculty of Medicine, Saga, Japan. Oncology Reports (2005), 13(5), 899-906. Publisher: Oncology Reports, CODEN: OCRPEW ISSN: 1021-335X. Journal written in English. CAN 143:638 AN 2005:407240 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

O6-Me guanine methyltransferase (MGMT) repairs O6-alkylguanine in cellular DNA introduced by the clin. used alkylating drug 1-(4-amino-2-methyl-5-pyrimidinyl) methyl-3-(2-chloroethyl)-3-nitrosourea (ACNU). Thus, cancer cells with MGMT expression are

resistant to ACNU treatment. Cisplatin has been reported to suppress MGMT expression; however, the mol. mechanism by which cisplatin reduces MGMT expression remains to be elucidated. Using gallbladder cancer cells (KMG-C) expressing MGMT, we analyzed whether a low dose of cisplatin suppresses MGMT expression, followed by an enhanced drug effect of ACNU in vitro and in vivo. We also investigated the promoter region crit. for the transcriptional repression of MGMT gene by cisplatin using 5 deletion mutants in reporter promoter assays. In RT-PCR anal., the expression of MGMT mRNA in KMG-C cells was dose- and time-dependently repressed. Drug sensitivity to ACNU was increased 2-fold by pretreatment with cisplatin, compared with only ACNU treatment, in MTT assays as well as tumor-bearing nude mice. Although the 5'-flanking region is deleted as far as -69 bp upstream of the transcription start site, cisplatin dose dependently inhibited luciferase activity. However, cisplatin did not cause such repression when 59 bp region from -69 to -10 bp was deleted. We confirmed that cisplatin enhanced sensitivity to ACNU in KMG-C cells expressing MGMT both in vitro and in vivo. Furthermore, a low dose of cisplatin repressed the transcription of the MGMT promoter. The 59 bp region in the MGMT promoter was crucial for repression by cisplatin. These results might form the basis of a chemotherapeutic strategy involving alkylating agents via prior cisplatin-induced biochem. modulation.

Answer 41:

Bibliographic Information

Anticancer effect of an α-TEA liposome aerosol. Knight, Vernon. Molecular Physiology and Biophysics, Baylor College of Medicine, Houston, TX, USA. Experimental Biology and Medicine (Maywood, NJ, United States) (2005), 230(5), 291. Publisher: Society for Experimental Biology and Medicine, CODEN: EBMMBE ISSN: 1535-3702. Journal written in English. CAN 143:90407 AN 2005:392967 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The research of Anderson et al. (2004) entitled "α-TEA plus cisplatin reduced human cisplatin-resistant ovarian cancer cell tumor burden and metastasis" is reviewed with commentary and refs. α-TEA is a novel acetic acid analog of vitamin E in a liposome aerosol for anticancer treatment. Anderson et al. found that α-TEA, when given concurrently with cisplatin to mice, it significantly reduced tumor burden, lung metastases, and other aspects of cancer growth.

Answer 42:

Bibliographic Information

Enhanced sensitivity to the HER1/epidermal growth factor receptor tyrosine kinase inhibitor erlotinib hydrochloride in chemotherapy-resistant tumor cell lines. Dai, Qun; Ling, Yi-He; Lia, Marie; Zou, Yi-Yu; Kroog, Glenn; Iwata, Kenneth K.; Perez-Soler, Roman. Department of Oncology, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY, USA. Clinical Cancer Research (2005), 11(4), 1572-1578. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 143:37988 AN 2005:180845 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Erlotinib (Tarceva, OSI-774) is a potent and specific inhibitor of the HER1/epidermal growth factor receptor (EGFR) tyrosine kinase. In phase II clin. studies, oral erlotinib monotherapy has shown antitumor activity in patients with advanced non-small cell lung cancer, head and neck cancer, and ovarian cancer after the failure of std. chemotherapy. We hypothesized that some tumors treated with multiple cytotoxic therapies may become more dependent on the HER1/EGFR signaling pathways for survival. The growth-inhibitory effect of erlotinib was tested on 10 pairs of chemosensitive, parental, and chemoresistant tumor cell lines. Enhanced sensitivity to erlotinib was obsd. in the doxorubicin-resistant human breast cancer cell line MCF-7, paclitaxel-resistant human ovarian carcinoma cell line A2780, and cisplatin-resistant human cervical carcinoma cell line ME180. The IC50 values of erlotinib in the resistant cell lines were 2- to 20-fold lower than those in the corresponding parental cell lines. This enhanced sensitivity to erlotinib correlated with higher HER1/EGFR and phospho-HER1/EGFR expression when compared with the corresponding parental cell lines. Acquired resistance to cytotoxic agents was not assocd. with cross-resistance to erlotinib. AE-ME180/CDDP-resistant xenografts showed greater sensitivity

to erlotinib than parental ME180 xenografts did. Our findings suggest that acquired resistance to cytotoxic therapy in some tumors is assocd. with enhanced sensitivity to HER1/EGFR inhibitors, which correlates with increased HER1/EGFR expression. These data may explain some of the obsd. clin. activity of HER1/EGFR inhibitors in patients previously treated with multiple therapies. HER1/EGFR tyrosine kinase inhibitors may be more effective as second- or third-line treatment for certain patients with tumors that were previously treated with multiple chemotherapy regimens.

Answer 43:

Bibliographic Information

Preclinical evaluation of antisense bcl-2 as a chemosensitizer for patients with gastric carcinoma. Kim, Ryungsa; Emi, Manabu; Tanabe, Kazuaki; Toge, Tetsuya. Department of Surgical Oncology, Research Institute for Radiation Biology and Medicine, Hiroshima University, Hiroshima, Japan. Cancer (New York, NY, United States) (2004), 101(10), 2177-2186. Publisher: John Wiley & Sons, Inc., CODEN: CANCAR ISSN: 0008-543X. Journal written in English. CAN 142:253981 AN 2004:1061374 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

BACKGROUND: Because bcl-2 is a crit. factor for anticancer drug-induced apoptosis, the authors conducted a preclin. evaluation of antisense (AS) bcl-2 as an enhancer of the chemotherapeutic effect in the treatment of patients with gastric carcinoma. METHODS: AS bcl-2 was used with 18-mer phosphorothiated oligonucleotides in the MKN-45 gastric carcinoma cell line. Drug sensitivity in vitro was evaluated using the methyl-thiazoldiphenyl tetrazolium assay, and antitumor effects in vivo were evaluated using the nude mouse xenograft. Apoptosis was detd. with the terminal deoxyuridine triphosphate nick-end labeling assay. AS bcl-2 in vitro was treated with lipofectin, whereas it was administered i.p. for 6 consecutive days twice every 2 wk in vivo. Anticancer drugs were administered i.p. four times per wk. RESULTS: bcl-2 was down-regulated to 60% of its initial value after treatment with 1.0 μM AS bcl-2 compared with the controls of random and mismatched oligonucleotides. Drug sensitivity to doxorubicin, cisplatin, and paclitaxel (TXL) was increased 3-4-fold when used in combination with AS bcl-2, which was detd. with 50% inhibitory concn. values, compared with the control group. Increased drug sensitivity was assocd. with apoptosis, which increased in Bax and poly-ADP (ADP-ribose) polymerase and decreased in phosphorylated Akt (pAkt). The antitumor effect of cisplatin and TXL in vivo was enhanced significantly in combination with AS bcl-2. Down-regulation of bcl-2 was obsd. on Day 4 after the treatment with AS bcl-2. CONCLUSIONS: Combination treatment with AS bcl-2 and anticancer drugs, including cisplatin and TXL, may be a new strategy for enhancing chemotherapeutic effects in the treatment of gastric carcinoma.

Answer 44:

Bibliographic Information

Human osteosarcoma xenografts and their sensitivity to chemotherapy. Bruheim, Skjalg; Bruland, Oyvind S.; Breistol, Knut; Maelandsmo, Gunhild M.; Fodstad, Oystein. Department of Tumor Biology, Institute for Cancer Research, The Norwegian Radium Hospital, Oslo, Norway. Pathology Oncology Research (2004), 10(3), 133-141. Publisher: Aranyi Lajos Foundation, CODEN: POREFR ISSN: 1219-4956. Journal written in English. CAN 142:253924 AN 2004:1018322 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Despite the increased survival rates of osteosarcoma patients attributed to adjuvant chemotherapy, at least one third of the patients still die due to their disease. Further improvements in the management of osteosarcoma may rely on a more individualized treatment strategy, as well as on the introduction of new drugs. To aid in the preclin. evaluation of new candidate substances against osteosarcoma, we have established 11 human osteosarcoma xenograft lines and characterized them with regard to response to five different ref. drugs. Doxorubicin, cisplatin methotrexate, ifosfamide and lomustine were effective in 3/11, 3/11,1/10, 5/11 and 4/11 of the xenografts, resp. Five xenografts were resistant to all compds. tested. We also assessed the mRNA expression levels of the xenografts for the O6-Methylguanine DNA Methyltransferase (MGMT), DNA topoisomerase II- (Topo II)-α, Gluthathione-S-transferase

(GST)-π, Multidrug-resistance related protein (MRP) 1 and Multidrug-resistance (MDR) 1 genes. There was an inverse correlation between the transcript levels of GST-π and doxorubicin growth inhibition (r = -0.66; p<0.05), and between the transcript levels of MGMT and the effect of lomustine (r = -0.72; p<0.01), whereas the expression of MRP1 and cisplatin growth inhibition was pos. correlated (r=0.82; p<0.005). This panel of xenografts should constitute a good tool for pharmacol. and mol. studies in osteosarcoma.

Answer 45:

Bibliographic Information

Characterisation of molecular events following cisplatin treatment of two curable ovarian cancer models: contrasting role for p53 induction and apoptosis in vivo. Clarke, P. A.; Pestell, K. E.; Di Stefano, F.; Workman, P.; Walton, M. I. Cancer Research UK Centre for Cancer Therapeutics, Institute of Cancer Research, Haddow Laboratories, Sutton, Surrey, UK. British Journal of Cancer (2004), 91(8), 1614-1623. Publisher: Nature Publishing Group, CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 142:190391 AN 2004:834775 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The detailed mol. basis and determinants of in vivo tumor sensitivity to conventional anticancer agents remain unclear. We examd. the cellular and mol. consequences of cisplatin treatment using two ovarian tumor xenograft models that had not been previously adapted to culture in vitro. Both xenografts were curable with clin. relevant multiple doses of cisplatin. Following a single dose of cisplatin (6 mg kg-1 i.p.) growth delays of 25 and 75 days were obtained for pxn100 and pxn65, resp. This difference in response was not due to differences in DNA damage. Pxn100 tumors had a functional p53 response and a wild-type p53 sequence, whereas pxn65 harbored a mutant p53 and lacked a functional p53 response. Microarray anal. revealed the induction of p53-regulated genes and regulators of checkpoint control and apoptosis in pxn100 tumors following cisplatin-treatment. By contrast, there was no p53-dependent response and only limited changes in gene expression were detected in the pxn65 tumors. TUNEL anal. demonstrated high levels of apoptosis in the pxn100 tumors following cisplatin treatment, but there was no detectable apoptosis in the pxn65 tumors. Our observations show that a marked in vivo response to cisplatin can occur via p53-dependent apoptosis or independently of p53 status in human ovarian xenografts.

Answer 46:

Bibliographic Information

No topoisomerase I alteration in a neuroblastoma model with in vivo acquired resistance to irinotecan. Calvet, L.; Santos, A.; Valent, A.; Terrier-Lacombe, M-J.; Opolon, P.; Merlin, J-L.; Aubert, G.; Morizet, J.; Schellens, J. H. M.; Benard, J.; Vassal, G. Pharmacology and New Treatments in Cancer (UPRES EA 3535), Institut Gustave-Roussy, Villejuif, Fr. British Journal of Cancer (2004), 91(6), 1205-1212. Publisher: Nature Publishing Group, CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 142:169216 AN 2004:824732 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

CPT-11 (irinotecan) is a DNA-topoisomerase I inhibitor with preclin. activity against neuroblastoma (NB) xenografts. The aim was to establish in vivo an NB xenograft resistant to CPT-11 in order to study the resistance mechanisms acquired in a therapeutic setting. IGR-NB8 is an immature NB xenograft with MYCN amplification and 1p deletion, which is sensitive to CPT-11. Athymic mice bearing advanced-stage s.c. tumors were treated with CPT-11 (27 mg kg-1 day-1 × 5) every 21 days (1 cycle) for a max. of four cycles. After tumor regrowth, a new in vivo passage was performed and the CPT-11 treatment was repeated. After the third passage, a resistant xenograft was obtained (IGRNB8-R). The tumor growth delay (TGD) was reduced from 115 at passage 1 to 40 at passage 4 and no complete or partial regression was obsd. After further exposure to the drug, up to 28 passages, the resistant xenograft was definitively established with a TGD from 17 at passage 28. Resistant tumors reverted to sensitive tumors after 15 passages without treatment. IGR-NB8-R remained sensitive to cyclophosphamide and cisplatin and cross-resistance was obsd. with the topoisomerase I inhibitor topotecan. No quant. or qual. topoisomerase I modifications were obsd. The level of expression of multidrug resistance 1 (MDR1), MDR-assocd. protein 1 (MRP1) and, breast cancer resistance protein, three members of the ATP-binding cassette transporter

family was not modified over passages. Our results suggest a novel resistance mechanism, probably not involving the mechanisms usually obsd. in vitro.

Answer 47:

Bibliographic Information

Effect on Tumor Cells of Blocking Survival Response to Glucose Deprivation. Park, Hae-Ryong; Tomida, Akihiro; Sato, Shigeo; Tsukumo, Yoshinori; Yun, Jisoo; Yamori, Takao; Hayakawa, Yoichi; Tsuruo, Takashi; Shin-ya, Kazuo. Laboratory of Chemical Biology, The University of Tokyo, Bunkyo-ku, Tokyo, Japan. Journal of the National Cancer Institute (2004), 96(17), 1300-1310. Publisher: Oxford University Press, CODEN: JNCIEQ ISSN: 0027-8874. Journal written in English. CAN 142:126800 AN 2004:748256 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Background: Glucose deprivation, a feature of poorly vascularized solid tumors, activates the unfolded protein response (UPR), a stress-signaling pathway, in tumor cells. We recently isolated a novel macrocyclic compd., versipelostatin (VST), that inhibits transcription from the promoter of GRP78, a gene that is activated as part of the UPR. We examd. the effect of VST on the UPR induced by glucose deprivation or other stressors and on tumor growth in vivo. Methods: Human colon cancer HT-29, fibrosarcoma HT1080, and stomach cancer MKN74 cells were cultured in the absence of glucose or in the presence of glucose and a UPR-inducing chem. stressor (the N-glycosylation inhibitor tunicamycin, the calcium ionophore A23187, or the hypoglycemia-mimicking agent 2-deoxyglucose [2DG]). The effect of VST on UPR induction was detd. by reverse transcription-polymerase chain reaction and immunoblot anal. of the UPR target genes GRP78 and GRP94; by immunoblot anal. of the UPR transcriptional activators ATF6, XBP1, and ATF4; and by analyzing reporter gene expression in cells transiently transfected with a GRP78 promoter-reporter gene. Cell sensitivity to VST was examd. with a colony formation assay and flow cytometry. In vivo antitumor activity of VST was assessed with an MKN74 xenograft model. Results: VST inhibited expression of UPR target genes in glucose-deprived or 2DG-treated cells but not in cells treated with tunicamycin or A23187. VST also inhibited the prodn. of the UPR transcriptional activators XBP1 and ATF4 during glucose deprivation. The UPR-inhibitory action of VST was seen only in conditions of glucose deprivation and caused selective and massive killing of the glucose-deprived cells. VST alone and in combination with cisplatin statistically significantly (P = .004 and P<.001 for comparisons with untreated control, resp.) inhibited tumor growth of MKN74 xenografts. Conclusion: Disruption of the UPR may provide a novel therapeutic approach to targeting glucose-deprived solid tumors.

Answer 48:

Bibliographic Information

Low toxicity and anticancer activity of a novel liposomal cisplatin (Lipoplatin) in mouse xenografts. Boulikas, Teni. Regulon, Inc., Mountain View, CA, USA. Oncology Reports (2004), 12(1), 3-12. Publisher: Oncology Reports, CODEN: OCRPEW ISSN: 1021-335X. Journal written in English. CAN 142:85988 AN 2004:583889 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Cisplatin has been one of the most widely used and most effective cytotoxic agents in the treatment of malignancies but causes severe adverse reactions including nausea/vomiting, renal toxicity, gastrointestinal toxicity, peripheral neuropathy, asthenia, and ototoxicity. A liposomal formulation of cisplatin, Lipoplatin, was developed in order to reduce the systemic toxicity of cisplatin. A single treatment of rats with 30 mg/kg Lipoplatin resulted in no toxicity whereas 2 or 3 weekly administrations at 30 mg/kg to rats gave neutropenia but no nephrotoxicity. On the contrary, a single injection to rats of 5 mg/kg cisplatin resulted in severe nephrotoxicity. Thus, Lipoplatin is less toxic than cisplatin in rats. I.p. or i.v. injection of Lipoplatin to SCID (severe combined immunodeficient) mice with s.c. breast MCF-7 or prostate LNCaP human tumors resulted in size redn. of the tumors; histol. examn. of the treated tumors in xenografts was consistent with apoptosis in tumor cells; thus, Lipoplatin appears to exert its cytotoxic effects to tumors in a mechanism similar to that of cisplatin. The preclin. studies reported here set the foundation for the clin. use of Lipoplatin as an

exciting new drug with lower toxicity than cisplatin, endowed with proapoptotic properties.

Answer 49:

Bibliographic Information

Changes in thymidylate synthase and its inhibition rate and changes in dihydropyrimidine dehydrogenase after the administration of 5-fluorouracil with cisplatin to nude mice with gastric cancer xenograft SC-1-NU. Sakurai, Yoichi; Uraguchi, Takashi; Imazu, Hiroki; Hasegawa, Shigeru; Matsubara, Toshiki; Ochiai, Masahiro; Funabiki, Takahiko. Department of Surgery, Fujita Health University School of Medicine, Toyoake, Aichi, Japan. Gastric Cancer (2004), 7(2), 110-116. Publisher: Springer-Verlag Tokyo, CODEN: GCANFO ISSN: 1436-3291. Journal written in English. CAN 142:106640 AN 2004:525683 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Although 5-fluorouracil (5-FU) and cis-diamminedichloroplatinum (cisplatin) in combination have synergistic cytotoxicity against both murine and human neoplasms, the precise mechanism of the synergism, and the effects on thymidylate synthase (TS) and its percent inhibition, and the effects on dihydropyrimidine dehydrogenase (DPD) remained to be elucidated. Exptl. chemotherapy was performed using SC-1-NU, a human gastric carcinoma xenograft. SC-1-NU was maintained by serial transplantation in male BALB/c nude mice. The nude mice received various chemotherapeutic regimens consisting of 5-FU and/or cisplatin, with different dosages and periods of administration. After the treatment, we examd. the in vivo effects of 5-FU and cisplatin in each regimen on thymidylate synthase and its percent inhibition, and the effects on DPD, in addn. to the observation of tumor growth inhibition. The combined use of 5-FU (20 mg/kg per day) and cisplatin (either 1.5 or 7.5 mg/kg per day) showed a synergistic antitumor effect, regardless of the different doses of cisplatin. The long-term administration of 5-FU significantly increased both total thymidylate synthase and the percent thymidylate synthase inhibition rate. The short-term administration of 5-FU significantly decreased DPD. Nevertheless, these changes showed no relation to the combined use of cisplatin. Combined administration of cisplatin with 5-FU did not further increase thymidylate synthase inhibition over that occurring with 5-FU alone, which does not support the hypothesis that cisplatin combined with 5-FU modulates thymidylate synthase inhibition in enhancing the anticancer effect of 5-FU. Changes in DPD after the administration of 5-FU may provide an insight into tumor sensitivity and resistance to 5-FU.

Answer 50:

Bibliographic Information

Selective modulation of the therapeutic efficacy of anticancer drugs by selenium containing compounds against human tumor xenografts. Cao, Shousong; Durrani, Farukh A.; Rustum, Youcef M. Department of Pharmacology and Therapeutics, Roswell Park Cancer Institute, Buffalo, NY, USA. Clinical Cancer Research (2004), 10(7), 2561-2569. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 141:360262 AN 2004:290939 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Studies were carried out in athymic nude mice bearing human squamous cell carcinoma of the head and neck (FaDu and A253) and colon carcinoma (HCT-8 and HT-29) xenografts to evaluate the potential role of selenium-contg. compds. as selective modulators of the toxicity and antitumor activity of selected anticancer drugs with particular emphasis on irinotecan, a topoisomerase I poison. Antitumor activity and toxicity were evaluated using nontoxic doses (0.2 mg/mouse/day) and schedule (14-28 days) of the selenium-contg. compds., 5-methylselenocysteine and seleno-L-methionine, administered orally to nude mice daily for 7 days before i.v. administration of anticancer drugs, with continued selenium treatment for 7-21 days, depending on anticancer drugs under evaluation. Several doses of anticancer drugs were used, including the max. tolerated dose (MTD) and toxic doses. Although many chemotherapeutic agents were evaluated for toxicity protection by selenium, data on antitumor activity were primarily obtained using the MTD, 2 x MTD, and 3 x MTD of weekly x4 schedule of irinotecan. Selenium was highly protective against toxicity induced by a variety of chemotherapeutic agents. Furthermore, selenium increased significantly the cure rate of xenografts bearing human tumors

that are sensitive (HCT-8 and FaDu) and resistant (HT-29 and A253) to irinotecan. The high cure rate (100%) was achieved in nude mice bearing HCT-8 and FaDu xenografts treated with the MTD of irinotecan (100 mg/kg/wk x 4) when combined with selenium. Administration of higher doses of irinotecan (200 and 300 mg/kg/wk x 4) was required to achieve high cure rate for HT-29 and A253 xenografts. Administration of these higher doses was possible due to selective protection of normal tissues by selenium. Thus, the use of selenium as selective modulator of the therapeutic efficacy of anticancer drugs is new and novel.
We demonstrated that selenium is a highly effective modulator of the therapeutic efficacy and selectivity of anticancer drugs in nude mice bearing human tumor xenografts of colon carcinoma and squamous cell carcinoma of the head and neck. The obsd. in vivo synergic interaction is highly dependent on the schedule of selenium.

Answer 51:

Bibliographic Information

Clonogenic assay with established human tumour xenografts: correlation of in vitro to in vivo activity as a basis for anticancer drug discovery. Fiebig, H. H.; Maier, A.; Burger, A. M. Oncotest GmbH, Institute for Experimental Oncology, Freiburg, Germany. European Journal of Cancer (2004), 40(6), 802-820. Publisher: Elsevier Science Ltd., CODEN: EJCAEL ISSN: 0959-8049. Journal written in English. CAN 141:342988 AN 2004:284718 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Pluripotent cells can be grown in clonogenic assays. The tumor stem-cell fraction, which accounts for <0.4% of the total cells, and which is considered the most relevant cell type in the development of metastases and recurrences, is able to divide and to form colonies in a semisolid matrix (agar or methylcellulose). Major applications of the tumor clonogenic assay (TCA) are chemosensitivity testing of tumors and xenografts, and for assessments within drug discovery programs. Of crit. relevance for the usefulness of the TCA is whether it can predict sensitivity or resistance towards clin. used agents. When we compared the response of human tumors established as xenografts in nude mice in the TCA in vitro to that of the clin. response, 62% of the comparisons for drug sensitivity, and 92% of the comparisons for drug resistance were correct. The same percentage of true/false observations was found when tumors were tested after serial passage in nude mice in the TCA in vitro and their response compared to in vivo activity in corresponding xenografts (60% and 90%, resp.). The highest correct predictive values were, however, found when the clin. response of tumors was compared to their explants established in the nude mouse and treated in vivo. Of 80 comparisons performed, we obsd. a correct prediction for tumor resistance in 97% and for tumor sensitivity in 90%. In our opinion, the TCA with established human tumor xenografts has an important role in current drug discovery strategies. We therefore included the TCA as secondary assay in our approach to anticancer drug discovery and found that a no. of novel agents were active; these are now in advanced preclin. development or clin. trials. Thus, the tumor clonogenic assay has proven predictive value in the chemosensitivity testing of std. and exptl. anticancer drugs.

Answer 52:

Bibliographic Information

Improved targeting of platinum chemotherapeutics the antitumor activity of the HPMA copolymer platinum agent AP5280 in murine tumour models. Lin, X.; Zhang, Q.; Rice, J. R.; Stewart, D. R.; Nowotnik, D. P.; Howell, S. B. Department of Medicine and the Cancer Center, University of California, La Jolla, CA, USA. European Journal of Cancer (2004), 40(2), 291-297. Publisher: Elsevier Science Ltd., CODEN: EJCAEL ISSN: 0959-8049. Journal written in English. CAN 141:150527 AN 2004:34766 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

AP5280 is a novel N-(2-hydroxypropyl)methacrylamide (HPMA) copolymer-bound platinum (Pt) therapeutic designed to increase the therapeutic index relative to conventional, small-mol. platinum agents. The platinum-polymer construct accumulates in solid tumors on the basis of increased capillary permeability. The bound platinum moiety is present as an N,O-Pt chelate at the distal end of a

tetrapeptide linker, glycine-phenylalanine-leucine-glycine, and the wt.-av. mol. wt. (Mw) of the construct is 22 kDa. The antitumor activity and toxicity of AP5280 were assessed in the syngeneic murine B16F10 and Lewis lung tumor models, and in the human ovarian carcinoma 2008 and head and neck squamous carcinoma UMSCC10b xenograft models. The max. tolerated dose (MTD) of AP5280 was 6-fold greater than that of carboplatin (CBDCA) in vivo. AP5280 was active in all four tumor models, and it displayed a higher therapeutic index than CBDCA in each of these tumor models. The antitumor effect of AP5280 given at 16% of its MTD was equiv. to that produced by a MTD of CBDCA. Thus, consistent with the design goal for this drug, and despite being less potent than CBDCA, AP5280 produced less systemic toxicity relative to its antitumor activity and thus has a greater therapeutic index. On the basis of the improved therapeutic index evidenced in these models, AP5280 has been advanced into clin. trials.

Answer 53:

Bibliographic Information

Anti-tumor effect of intraperitoneal administration of cisplatin-loaded microspheres to human tumor xenografted nude mice.
Tamura, Takashi; Fujita, Fumiko; Tanimoto, Masahiko; Koike, Masako; Suzuki, Akira; Fujita, Masahide; Horikiri, Yuji; Sakamoto, Yasuo; Suzuki, Takehiko; Yoshino, Hiroyuki. DDS Research Department, Discovery Research Laboratory, Tanabe Seiyaku Co. Ltd., Yodogawa-ku, Osaka, Japan. Journal of Controlled Release (2002), 80(1-3), 295-307. Publisher: Elsevier Science Ltd., CODEN: JCREEC ISSN: 0168-3659. Journal written in English. CAN 138:147233 AN 2002:258837 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

This study evaluates the anti-tumor effect of cisplatin-loaded microspheres (CDDP-MS) against peritoneal carcinomatosis using human tumor xenografts. The incorporated CDDP was released from CDDP-MS for 3 wk in vivo as well as in vitro. CDDP-MS at a dose of 35 mg/kg (at maximal tolerable dose (MTD)) showed effective anti-tumor activity (tumor growth inhibition rate (IR)=70.3%) against Li-7 (human liver cancer) xenografts transplanted into the peritoneal cavity. This procedure also resulted in increased life span (ILS (%)=47.2%), whereas CDDP dissolved in saline soln. (CDDP-SOL) at a dose of 8 mg/kg (at MTD) was ineffective (IR=15.7%, ILS=2.6%). Likewise, CDDP-MS (35 mg/kg) significantly prolonged the mean survival time (ILS=50.8%) compared with a CDDP-SOL group (8 mg/kg) (ILS=13.1%) in the mice with Li-7 xenografts transplanted into the spleen. Furthermore, CDDP-MS showed markedly effective anti-tumor activity (IR=82.2%) against H-154 (human stomach cancer) xenografts, in which CDDP-SOL was effective (IR=69.5%) at the MTDs. The suppressive effect of CDDP-MS on accumulation of malignant ascites was intimately related to unchanged CDDP concn. in ascites. These results demonstrated that the administration of CDDP-MS resulted in an unchanged CDDP concn. in ascites, and induced a sustained tumor growth inhibition along with a prolonged survival time.

Answer 54:

Bibliographic Information

Bcl-2 antisense oligonucleotides chemosensitize human gastric cancer in a SCID mouse xenotransplantation model.
Wacheck, Volker; Heere-Ress, Elisabeth; Halaschek-Wiener, Julius; Lucas, Trevor; Meyer, Hildegard; Eichler, Hans-Georg; Jansen, Burkhard. Department of Clinical Pharmacology, Section of Experimental Oncology/Molecular Pharmacology, University of Vienna, Vienna, Austria. Journal of Molecular Medicine (Berlin, Germany) (2001), 79(10), 587-593. Publisher: Springer-Verlag, CODEN: JMLME8 ISSN: 0946-2716. Journal written in English. CAN 137:119152 AN 2002:4584 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

We used Bcl-2 antisense oligonucleotides (G3139) to chemosensitize human gastric cancer by down-regulation of Bcl-2 expression in vivo. Oligonucleotides and cisplatin were administered systemically in a human gastric cancer SCID mouse model, and Bcl-2 expression, apoptosis, tumor size, and survival were assessed. Used alone, G3139 treatment led to down-regulation of Bcl-2 and moderate tumor redn. compared to saline control. G3139 combined with cisplatin treatment markedly enhanced the antitumor effect of cisplatin (70% tumor size redn. vs. cisplatin alone), assocd. with increased apoptosis measured in tumor biopsy specimens. Combined

treatment with G3139 and cisplatin prolonged survival of the tumor-bearing SCID mice by more than 50% without adding significant drug-related toxicity. Treatment with Bcl-2 antisense oligonucleotides is thus a promising novel approach to enhance antitumor activity of cisplatin or other drugs used in gastric cancer therapy and warrants further evaluation in clin. trials.

Answer 55:

Bibliographic Information

Recombinant CD40 ligand therapy has significant antitumor effects on CD40-positive ovarian tumor xenografts grown in SCID mice and demonstrates an augmented effect with cisplatin. Ghamande, Sharad; Hylander, Bonnie L.; Oflazoglu, Ezogelin; Lele, Shashikant; Fanslow, William; Repasky, Elizabeth A. Departments of Surgery, Division of Gynecologic Oncology, Roswell Park Cancer Center, Buffalo, NY, USA. Cancer Research (2001), 61(20), 7556-7562. Publisher: American Association for Cancer Research, CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 136:112321 AN 2001:790237 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

CD40 is a member of the tumor necrosis factor receptor family and was first identified with a monoclonal antibody raised against bladder carcinoma. Recombinant human CD40L has been shown previously to have a direct antitumor effect on an ovarian cancer cell line and ovarian carcinoma cells isolated from ascites fluid. We show here that rhuCD40L inhibits the growth of several ovarian adenocarcinomas derived from surgical specimens and grown as xenografts in severe combined immunodeficient mice. Two 14-day treatment cycles were more effective than one. This effect is apparently not mediated by natural killer cells, because blocking natural killer cell activity by anti-asialo GM-1 did not diminish this effect. In addn. to suppression of tumor growth, treatment with rhuCD40L resulted in an increased expression of FasL, an increase in apoptosis, and histol. changes including increased fibrosis and areas of tumor destruction. Using this model, we examd. the efficacy of rhuCD40L in combination with chemotherapeutic agents. The antitumor effect of rhuCD40L in combination with 4 mg/kg cisplatin (CDDP) was increased over the effect of CDDP alone. Furthermore, rhuCD40L increased the efficacy of a suboptimal dose of CDDP (2 mg/kg) such that it matched that of high-dose CDDP alone. These data suggest a role for rhuCD40L therapy in combination with platinum based regimens for primary treatment of epithelial ovarian tumors.

Answer 56:

Bibliographic Information

Experimental chemotherapy against canine mammary cancer xenograft in SCID mice and prediction of its clinical effect. Yamashita, Atsuko; Maruo, Kohji; Suzuki, Kaoru; Shirota, Kinji; Kobayashi, Kimio; Hioki, Kyoji. Department of Veterinary Surgery, Tokyo University of Agriculture and Technology, Tokyo, Japan. Journal of Veterinary Medical Science (2001), 63(8), 831-836. Publisher: Japanese Society of Veterinary Science, CODEN: JVMSEQ ISSN: 0916-7250. Journal written in English. CAN 136:379575 AN 2001:706827 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effectiveness of 6 antitumor agents was evaluated for a canine mammary gland tumor (CMG-6) serially transplanted into mice with severe combined immunodeficiency. CMG-6, a solid carcinoma, was s.c. transplanted into immunodeficient mice, and 6 antitumor agents were given i.v. as a single injection. The min. EDs (MEDs; mg/kg) in mice were: cyclophosphamide (CPM) 65, doxorubicin (DXR) 6, cisplatin (CDDP) 5, vincristine (VCR) 1.6, vinblastine (VLB) >5.5, 5-fluorouracil (5-FU) 105. The clin. effects of the drugs were predicted based on the ratio of the area under the curve (AUC) in dogs given a clin. dose (AUC dog) to the AUC of mice given a MED (AUC mouse) from published refs. The AUC ratios were: CPM 2.24, DXR 0.19, CDDP 1.20, VCR 0.04, VLB <1.24 and 5-FU 1.15. The drugs having a value of >1.0 for the AUC dog/AUC mouse ratio were CPM, CDDP and 5-FU, suggesting that they might be effective in the original dogs with CMG-6. Combination chemotherapy using clin. equiv. doses of CDDP and CPM, which had the two highest values of the AUC dog/AUC mouse ratio in single-agent therapy, had addnl. effects as compared to the effectiveness of the single agents against CMG-6.

Answer 57:

Bibliographic Information

Anticancer effects of 5-fluorouracil combined with cisplatin using gastrointestinal cancer xenografts transplanted into nude mice. Uraguchi, Takashi; Sakurai, Yoichi; Nakayama, Kunihisa; Nozoe, Yasutomo; Kobayashi, Hidetaka; Shoji, Mitsutaka; Jinbo, Yasuko; Kanno, Osamu; Uchimura, Masashi; Imazu, Hiroki; Hasagawa, Shigeru; Matsubara, Toshiki. Dept. of Surgery, Fujita Health University School of Medicine, Japan. Fujita Gakuen Igakkaishi (2000), 24(1), 85-89. Publisher: Fujita Gakuen Igakkai, CODEN: FGIGDO ISSN: 0288-5441. Journal written in Japanese. CAN 134:336043 AN 2000:839934 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The anticancer effects of 5-fluorouracil combined with cisplatin were better than that of each drug alone, as studied by using gastrointestinal cancer xenografts transplanted into nude mice.

Answer 58:

Bibliographic Information

Antitumor effects of TZT-1027, a novel dolastatin 10 derivative, on human tumor xenografts in nude mice. Fujita, Fumiko; Koike, Masako; Fujita, Masahide; Sakamoto, Yasuo; Tsukagoshi, Shigeru. Experimental Cancer Chemotherapy Research Laboratory Co., Ltd., Japan. Gan to Kagaku Ryoho (2000), 27(3), 451-458. Publisher: Gan to Kagaku Ryohosha, CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 133:99219 AN 2000:263094 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

TZT-1027 was evaluated for its antitumor effects in sixteen human tumors xenografted in nude mice from gastric (H-81, H-106, H-30, H-154), breast (H-31, H-62), colon (H-110, H-143), lung (LC-376, H-74, Mqnu-l, LC-351), liver (H-181), renal cell (H-12) and ovarian (H-OC-3, COC-4) cancer lines. In the latter three and lung (Mqnu-1, LC-351) cancers the results were compared with those obtained with CPT-11, vincristine (VCR), CDDP, adriamycin (ADM). TZT-1027 showed effective antitumor activity (IR≥58%) against fifteen of the tumor lines, all but LC-351, and showed markedly effective activity (IR≥80%) against twelve tumor lines, including drug-resistant colon (H-110); lung (H-74) and ovarian (SOC-4) cancer lines. The complete regression was shown in five H-OC-3 tumor-bearing mice out of seven. Moreover, TZT-1027 was shown to be more potent in three cancer models (Mqnu-1, h-81, SOC-4) than CPT-11, and to have markedly effective antitumor activity in two cancers (H-12, H-OC-3) in which VCR was ineffective and in ovarian cancer (SOC-4) in which CPT-11, CDDP and ADM were ineffective. The administration of TZT-1027 induced fewer side effects; transient redn. of body wt. was obsd. in four lines out of sixteen tested. These results suggest that TZT-1027 is an excellent candidate for clin. trials for the treatment of cancer.

Answer 59:

Bibliographic Information

Development of human lymphoma/leukemia xenograft models in immune-deficient mice for evaluation of potential anticancer agents. Dykes, D. J.; Hollingshead, M. G.; Camalier, R. F.; Waud, W. R.; Mayo, J. G. Southern Research Institute, Birmingham, AL, USA. Contributions to Oncology (1999), 54(Relevance of Tumor Models for Anticancer Drug Development), 295-304. Publisher: S. Karger AG, CODEN: COONEV ISSN: 0250-3220. Journal written in English. CAN 133:217399 AN 2000:242563 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Eleven human lymphoma/leukemia cell lines were assessed as in vivo xenograft models in severe combined immunodeficient (SCID) mice. In prepn. for efficacy evaluations of new antitumor agents, all eleven cell lines have been characterized for sensitivity to known clin. useful agents. The lines included in the study represent a variety of diseases including T-cell, myelogenous, and lymphoblastic leukemias, as well as histiocytic, B-cell and Burkitt's lymphomas. The selected agents for this study were representative of various chem. classes. Addnl., growth studies were performed including comparisons in athymic nude mice. These studies were designed to det. s.c. tumor vol. doubling times, graft success, latent growth periods, and other characteristics necessary to effectively implement and interpret anticancer efficacy evaluations. The various tumor lines used proved to be good models for chemotherapy trials. In the chemotherapy trials, considerable independent chemotherapeutic profiles were obsd. but there were also some similarities among the various histol. types.

Answer 60:

Bibliographic Information

Evaluation of antitumor activity of etoposide administered orally for 21 consecutive days against human uterine cancer subcutaneous and/or orthotopic xenografts in nude mice. Matsumoto, Sayuri; Mashiba, Hiroko; Okamoto, Kazuya; Ekimoto, Hisao. Anticancer Drugs Dept., Research & Development Division, Pharmaceutical Group, Nippon Kayaku Co., Ltd, Japan. Gan to Kagaku Ryoho (1999), 26(9), 1313-1320. Publisher: Gan to Kagaku Ryohosha, CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 132:117203 AN 1999:634564 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor activity of etoposide (ETP) against human uterine cancer cell lines were investigated in vitro and in vivo. The cytotoxic activity of ETP against HeLa S3, a human cervical cancer cell line, depended on exposure time. The survival rate with 24 h prolonged exposure was reduced to about 1/200 that with 6 h exposure. The time dependency of antitumor activity of ETP against HeLa S3 s.c. transplanted in nude mice was studied. The effect of 21 or 28 consecutive days oral administration was greater than that of 5 or 14 consecutive days. Furthermore, a longer administration schedule was less toxic. The antitumor activity of ETP administered orally for 21 consecutive days was compared with that of CDDP, CPT-11 and 5'-DFUR using both human uterine cancer cell lines (TCO-1, SIHA, UCC08JCK) transplanted s.c. in nude mice and human uterine cancer cell lines (HeLa S3, UCC08JCK) transplanted into the uterus of nude mice. ETP showed the same antitumor activity as CPT-11 and 5'-DFUR against TCO-1 and UCC08JCK, human uterine cancer cell lines transplanted s.c. in nude mice. ETP also showed anticancer activity against two cell lines transplanted into the uterus. The growth inhibition caused by ETP administered orally at 50 mg/kg against HeLa S3 transplanted s.c. was 36.7% while that against the same cell line transplanted into the uterus was 58.5%. 5'-DFUR also showed the same antitumor activity as ETP. These results suggest that long term oral administration of ETP is clin. useful for cervical cancer patients.

Answer 61:

Bibliographic Information

Cisplatin and mitomycin C combination chemotherapy against human pancreatic cancer xenografts transplanted in nude mice. Tomikawa, Moriaki. School of Medicine, Department of Surgery, Keio University, Japan. Keio Igaku (1998), 75(6), T537-T545. Publisher: Keio Igakkai, CODEN: KEIGAS ISSN: 0368-5179. Journal written in Japanese. CAN 130:246421 AN 1999:16181 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Cisplatin and mitomycin C combination chemotherapy inhibited human pancreatic cancer xenografts transplanted in nude mice. The in vitro studies also indicated that the combination chemotherapy is clin. useful for treatment of pancreatic cancer.

Answer 62:

Bibliographic Information

Altered expression of resistance associated genes in hepatoblastoma xenografts incorporated into mice following treatment with adriamycin or cisplatin. Bader, Peter; Fuchs, Jorg; Wenderoth, Marc; Von Schweinitz, Dietrich; Niethammer, Dietrich; Beck, James F. Department Hematology and Oncology, University Children's Hospital, Tubingen, Germany. Anticancer Research (1998), 18(4C), 3127-3132. Publisher: Anticancer Research, CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 129:310505 AN 1998:559967 CAPLUS

Abstract

To study the development of drug resistance in childhood hepatoblastoma (HB) using a model closely related to in vivo conditions, we cultivated HB xenografts from 3 patients into mice and treated these tumors with either adriamycin (ADR) or cisplatin (CIS). Detn. of the relative expression levels of various resistance assocd. genes by a cDNA-PCR approach showed that significantly enhanced MDR1 gene expression levels after treatment with ADR in each case. Significantly enhanced glutathione S-transferase μ (GSTμ) gene expression levels after treatment with CIS in 2/3 xenografts. Significantly decreased levels of topoisomerase IIa (TOPO IIa) in tumors of the same two patients after treatment with either ADR or CIS. These findings give evidence that the MDR1-, GSTμ- and TOPO IIa-gene products may contribute to drug resistance in HB.

Answer 63:

Bibliographic Information

Antitumor effect of CPT-11, a camptothecin derivative, on human testicular tumor xenografts in nude mice. Miki, Tsuneharu; Sawada, Masumi; Nonomura, Norio; Kojima, Yasuyuki; Okuyama, Akihiko; Maeda, Osamu; Saiki, Shigeru; Kotake, Toshihiko. Department of Urology, Osaka University Medical School, Osaka, Japan. European Urology (1997), 31(1), 92-96. Publisher: S. Karger AG, CODEN: EUURAV ISSN: 0302-2838. Journal written in English. CAN 129:285665 AN 1998:542001 CAPLUS

Abstract

The antitumor effect of CPT-11, a camptothecin deriv., on two human testicular embryonal carcinomas (TTSC-2 and TTSC-3) heterotransplanted into nude mice was studied. Tumor-bearing nude mice were given daily i.p. injections of the anticancer drugs in 0.1 mL saline 3 times at 3-day intervals. At the end of the expts. tumors were resected and subjected to light-microscopic observation. When 10, 30 and 50 mg/kg of CPT-11 was administered to tumor-bearing mice i.p., the antitumor effect of CPT-11 was obsd. dose-dependently in both TTSC-2 and TTSC-3. When 30 mg/kg of CPT-11 was administered in combination with CDDP, complete tumor regression was obsd. in both TTSC-2 and TTSC-3 tumors. Histol. findings correlated well with the decrease in tumor vol. of treated tumors. No mice died after treatment with CPT-11 in a single-agent and combination chemotherapy. Chemotherapy with CPT-11 was an effective and safe method against human testicular tumors heterotransplanted in nude mice.

Answer 64:

Bibliographic Information

Multidrug resistance genes (MRP) and MDR1 expression in small cell lung cancer xenografts: relationship with response to chemotherapy. Canitrot, Yvan; Bichat, Francis; Cole, Susan P. C.; Deeley, Roger G.; Gerlach, James H.; Bastian, Gerard; Arvelo, Francisco; Poupon, Marie-France. Cancer Research Laboratories, Queen's University, Kingston, ON, Can. Cancer Letters (Shannon, Ireland) (1998), 130(1,2), 133-141. Publisher: Elsevier Science Ireland Ltd., CODEN: CALEDQ ISSN: 0304-3835. Journal written in English. CAN 129:310474 AN 1998:497582 CAPLUS

Abstract

Intrinsic or acquired drug resistance is a major limiting factor of the effectiveness of chemotherapy. Increased expression of either the MRP gene or the MDR1 gene has been demonstrated to confer drug resistance in vitro. In this study, we examd. MRP and MDR1

gene expression in a panel of 17 small cell lung cancers (SCLC) xenografted into nude mice from treated and untreated patients using an RT-PCR technique. For some of them, the outcome of the corresponding patients was known and we related MDR1/MRP expression with the xenograft response to C'CAV (cyclophosphamide, cisplatin, adriamycin and etoposide) combined chemotherapy. Fifteen (88%) of the 17 cases of SCLC were found to be pos. for either MDR1 or MRP. MRP gene expression was present in 12 (71%) of 17 cases, whereas MDR1 gene expression was detected in eight (50%) of 16 cases. For six SCLC, the survival duration of patients differed, with three patients surviving for >30 mo after therapy. Among these six tumors, five expressed MRP and/or MDR1. These six xenografts responded to the C'CAV treatment but a significant rate of cure was obtained in only three cases. No obvious relationship was obsd. between the response to this treatment and MRP or MDR1 expression. However, the remarkably high levels and frequency of MRP expression in some SCLC samples indicate that future developments in chemotherapy of this tumor type should anticipate that drugs which are substrates of MRP may be of limited effectiveness.

Answer 65:

Bibliographic Information

Human ovarian cancer xenografts in nude mice: chemotherapy trials with paclitaxel, cisplatin, vinorelbine and titanocene dichloride. Vellena-Heinsen, C.; Friedrich, M.; Ertan, A. K.; Farnhammer, C.; Schmidt, W. Department Obstetrics Gynecology, University Saarland, Homburg/Saar, Germany. Anti-Cancer Drugs (1998), 9(6), 557-563. Publisher: Lippincott-Raven Publishers, CODEN: ANTDEV ISSN: 0959-4973. Journal written in English. CAN 129:225378 AN 1998:496740 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The new cytostatics titanocene dichloride and vinorelbine were compared to cisplatin and paclitaxel using a human ovarian cancer xenografts model. Biopsy material from a native human ovarian carcinoma was expanded and transplanted into 96 nude mice. The animals were divided into six treatment groups: cisplatin 3 × 4 mg/kg, paclitaxel 5 × 26 mg/kg, vinorelbine 1 × 20 mg/kg, titanocene dichloride 3 × 30 mg/kg, titanocene dichloride 3 × 40 mg/kg and a control group treated with 0.9% saline. Each expt. was repeated with eight mice in each treatment group. Treatment groups were evaluated in terms of av. daily increase in tumor vol. and av. daily body wt. increase of nude mice based on slopes of least-square regressions performed on individual animals. The slope factors α and β of the body wt. (α) and tumor vol. changes (β) within each group during the course of an expt. were calcd. Both a statistically significant decrease ($p<0.05$) in the body wt. of the exptl. animals (cisplatin: α=-0.5163, vinorelbine: α=-0.6598, paclitaxel: α=-0.6746, titanocene dichloride 3 × 30 mg/kg: α=-0.6259, titanocene dichloride 3 × 40 mg/kg: α=-0.7758) and a significant redn. ($p<0.05$) of the increase in tumor vol. (cisplatin: β=12.049, vinorelbine: β=0.504, paclitaxel: β=-1.636, titanocene dichloride 3 × 30 mg/kg: β=-6.212, titanocene dichloride 3 × 40 mg/kg: β=-0.685) was shown in all treated groups compared to the control group (α=-0.1398; β=23.056). No significant wt. changes were obsd. between the individually treated groups. A statistically significant redn. of the tumor growth occurred under paclitaxel (β=-1.636), vinorelbine (β=-0.504) and titanocene dichloride medication 3 × 40 mg/kg (β=-0.685), as compared to the group treated with cisplatin (β=-12.049). We found titanocene dichloride to be as effective as paclitaxel and more effective than cisplatin. Vinorelbine seems to be a very effective antineoplastic agent exhibiting a significant higher cytostatic effect than cisplatin.

Both titanocene dichloride and vinorelbine provide new therapeutic options in women with ovarian carcinoma not responding to std. chemotherapy.

Answer 66:

Bibliographic Information

Effectiveness of cisplatin, paclitaxel, and suramin against human malignant mesothelioma xenografts in athymic nude mice. Chahinian, A. Philippe; Mandeli, John P.; Gluck, Harry; Naim, Houshmand; Teirstein, Alvin S.; Holland, James F. Division of Neoplastic Diseases, Mount Sinai School of Medicine, New York, NY, USA. Journal of Surgical Oncology (1998), 67(2), 104-111. Publisher: Wiley-Liss, Inc., CODEN: JSONAU ISSN: 0022-4790. Journal written in English. CAN 128:252623 AN 1998:134707 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Malignant mesothelioma has a poor prognosis and is refractory to many agents. The antitumor effectiveness of cisplatin, paclitaxel, and suramin as single agents and in combination was evaluated in vivo against four lines of human pleural malignant mesothelioma xenografts in athymic nude mice, including one epithelial type and three fibrosarcomatous. After growth of tumors occurred by day 54 or 55, mice were randomized in groups of four each to receive either cisplatin 4 mg/kg i.p. weekly x5, or paclitaxel (Taxol) 12.5 mg/kg s.c. daily 5 days/wk for 3 consecutive weeks, or suramin 60 mg/kg i.p. daily x4,vs. controls treated with normal saline. Results: Cisplatin was very effective against one line and also to a lesser degree against another line. Paclitaxel showed antitumor effects similar to cisplatin, being very effective in one line, and also showed good activity in another line. Suramin was basically inactive in all four lines. Following the results obtained with these single agents, it was decided to evaluate the combination of cisplatin and paclitaxel, which resulted in more pronounced antitumor effect in all four cell lines. These results indicate that the combination of cisplatin and paclitaxel is superior to each agent alone in this model, and that it deserves to be evaluated in patients with malignant mesothelioma.

Answer 67:

Bibliographic Information

Antitumor effect of S-1 and cisplatin treatment against human gastric cancer xenografted in nude mice. Kondo, Ken; Akiyama, Seiji; Kasai, Yasushi; Kato, Sawako; Kuno, Yasushi; Kataoka, Masato; Ichihara, Tooru; Horisawa, Masumasa; Shirasaka, Tetsuhiko. Dept. Surgery II, Nagoya University School Medicine, Japan. Gan to Kagaku Ryoho (1997), 24(9), 1103-1108. Publisher: Gan to Kagaku Ryohosha, CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 127:214668 AN 1997:484469 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The enhanced effects due to the combined use of oral administration of S-1 and i.p. administration of cisplatin (CDDP) were examd. with gastric cancer xenografts (NUGC 4). S-1, a new anticancer drug, was daily administered at 10 mg/kg (qid×5×3 wk). 5-FU level in blood was 1 μg/mL at two hours after the treatment. Antitumor activity was not found in mice with only the CDDP treatment. But antitumor activity by S-1 and daily low-dose (1 mg/kg) or intermittent treatment (5 mg/kg) of CDDP showed better results than daily S-1 treatment. The daily low-dose CDDP treatment showed similar efficacy to the intermittent administration at the same total dose, but the daily low-dose CDDP treatment was better in the light of toxicities. These results suggest that treatment with S-1 and daily low-dose CDDP was effective for gastric cancer.

Answer 68:

Bibliographic Information

Influence of chemotherapy on FDG uptake by human cancer xenografts in nude mice. Yoshioka, Takashi; Takahashi, Hiromu; Oikawa, Hirosuke; Maeda, Syunichi; Ido, Tatuo; Akaizawa, Takashi; Fukuda, Hiroshi; Kanamaru, Ryunosuke. Dep. Clinical Oncology, Nuclear Medicine & Radiology, Inst. Development, Aging & Cancer, & Cyclotron & Radioisotope Center, Tohoku Univ., Sendai, Japan. Journal of Nuclear Medicine (1997), 38(5), 714-717. Publisher: Society of Nuclear Medicine, CODEN: JNMEAQ ISSN: 0161-5505. Journal written in English. CAN 126:327539 AN 1997:347780 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

This study evaluated the use of PET with 18F-2-deoxy-2-fluoro-D-glucose (18F-FDG) for monitoring chemotherapy effects, using a human cancer xenograft (poorly differentiated human gastric cancer) in vivo model. Tumor 18F-FDG uptakes and sizes were measured after administrating mitomycin (MMC), cisplatin (CDDP) and adriamycin (ADR) to xenograft-bearing nude mice and compared with 18F-FDG tumor uptake and tumor size in a non-therapy group. The correlation between the uptake and size was also assessed. The largest redn. in tumor size after chemotherapy occurred in the MMC administered group, followed by the CDDP case, with no redn. in the ADR groups as compared to the controls. Fluorine-18-FDG tumor uptake after chemotherapy was also decreased in the MMC and CDDP groups, in that order, but not in the ADR case. With MMC and CDDP, size redn. became significant on Days 8

or 11, whereas 18F-FDG tumor uptake had already been decreased on Day 3 or 7. Fluorine-18-FDG uptake decreases in parallel to the efficacy of anticancer agents and correlates with subsequent morphol. changes. We conclude that 18F-FDG PET tumor images are indeed useful for monitoring the effects of cancer chemotherapy.

Answer 69:

Bibliographic Information

Establishment and characterization of ovarian endometrioid adenocarcinoma cell line in nude mice and analyses of the immunohistochemical property among the original, recurred, and heterotransplanted tumor. Okina, Hideto; Kataoka, Akio; Sugiyama, Toru; Nishida, Takashi; Yakushiji, Michiaki. Departments of Obstetrics and Gynecology, Kurume University School of Medicine, Kurume, Japan. International Journal of Oncology (1997), 10(2), 311-316. Publisher: International Journal of Oncology, CODEN: IJONES ISSN: 1019-6439. Journal written in English. CAN 126:184525 AN 1997:144146 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The establishment and characterization of a new human endometrioid adenocarcinoma cell line (KOC-8e) derived from the malignant ascites is described. The original tumor at the initial operation showed pos. in TPA, and SLX immunohistochem. By contrast, recurred tumor showed pos. for CA125, TPA, SLX, MUC-1, and p53. In addn., the heterotransplanted tumor showed pos. for CA125, TPA, SLX, MUC-1, and p53. The DNA index was similar in the primary, recurred, and nude mouse tumor ranging between 1.93 and 2.05. The tumor growths were suppressed dose dependently by CDDP and CPT-11. CA125 showed useful as a tumor marker of this tumor, however, the nude mice had detectable tumor without elevation of CA125 after low dose application of CDDP and CPT-11. Thus, clin. detn. of chemotherapeutic effect and residual tumor cannot be made only by CA125. KOC-8e cells could be useful to study histol. anal. and chemosensitivity.

Answer 70:

Bibliographic Information

Dual biochemical modulation therapy using 5-FU, leucovorin and cisplatin on human rectal carcinoma xenografts in nude mouse. Shibusawa, Miki; Takata, Manabu; Kamiyama, Gouichi; Yokoyama, Noboru; Nakao, Kentaroh; Yoshizawa, Hiroto; Choh, Hirotoshi; Yasuda, Naokuni; Tsunoda, Yuko; et al. Dep. Surgery, Showa Univ. Sch. Med., Tokyo, Japan. Gan to Kagaku Ryoho (1996), 23(9), 1149-1152. Publisher: Gan to Kagaku Ryohosha, CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 125:185215 AN 1996:545435 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

This study examd. a combined treatment for colorectal carcinoma, the dual biochem. modulation therapy, consisting of 5-FU, Leucovorin (LV) and Cisplatin (CDDP). We compared the antitumor effects with other treatments: 5-FU alone, CDDP alone and 5-FU with LV. Primary diffuse infiltrated colorectal carcinoma is well known for its biol. malignancy and its lack of response to chemotherapy. We used SRM cells from a cell line of carcinoma of the rectum, and s.c. injected them into nude mice. The antitumor effects were estd. from the growth rate, inhibition rate and thymidylate synthetase inhibition rates in the tumor tissue. Results indicated that even if the concn. of 5-FU and LV were reduced by half, these combined with CDDP were more effective than other therapies. Dual biochem. modulation therapy is particularly promising because the redn. of the dosages would reduce the side effects while still serving as an excellent antitumor therapy.

Answer 71:

Bibliographic Information

Establishment and serial quantification of intrahepatic xenografts of human hepatocellular carcinoma in severe combined immunodeficiency mice, and development of therapeutic strategies to overcome multidrug resistance. Leveille-Webster, Cynthia R.; Arias, Irwin A. School Medicine, Tufts University, Boston, MA, USA. Clinical Cancer Research (1996), 2(4), 695-706. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 124:332166 AN 1996:261680 CAPLUS

Abstract

A murine model in which to study multiple drug resistance in human hepatocellular carcinoma was developed. PRF/PLC/5 hepatoma cells (Alex 0) and an induced multidrug resistant clone (Alex 0.5) were injected intrasplenically into severe combined immunodeficiency mice. In 70% of injected mice, hepatoma cells engrafted in the liver and grew as intrahepatic metastasis. Since Alex cells contain an integrated hepatitis B virus genome and secrete hepatitis B surface antigen (HBsAg), the serum HBsAg concn. in tumor-bearing mice was used to quantitate tumor burden. Tumor wet wt. detd. at necropsy was directly proportional to the serum HBsAg concn. In Alex 0 cells, IC50s for doxorubicin, vinblastine, and cis-platinum were 0.35 μM, 0.029 μM, and 3.70 μM, resp. Alex 0.5 cells were 25-, 14-, and 1.4-fold more resistant to doxorubicin, vinblastine, and cis-platinum, resp. Immunoblotting of Alex 0 cell membranes with an anti-P-glycoprotein antibody (C219) revealed small amts. of P-glycoprotein, whereas Alex 0.5 membranes overexpressed the protein. Concurrent exposure to verapamil (10 μM) sensitized both cell lines to the cytotoxic action of vinblastine and doxorubicin but had no effect on the cytotoxicity of cis-platinum. Mice bearing intrahepatic xenografts derived from Alex 0 and 0.5 cells had no response to treatment with i.v. vinblastine or doxorubicin, as was anticipated from in vitro drug testing. Addn. of verapamil to vinblastine treatment did not improve the success of in vivo chemotherapy. Immunotherapy with a human anti-P-glycoprotein antibody (MRK16) suppressed the in vivo growth of tumors derived from both cell lines. The effect was most pronounced in mice bearing Alex 0.5 tumors. Immunoblotting of tumors which initially responded to MRK16 therapy, but subsequently relapsed, revealed a marked decrease in P-glycoprotein expression when compared to results in tumors that were untreated or treated with vinblastine or control antibody.

In summary, we have developed an intrahepatic tumor xenograft model of human hepatocellular carcinoma in mice that permits noninvasive serial quantification of tumor burden by detn. of serum HBsAg levels and demonstrated a pos. response to immunotherapy with anti-P-glycoprotein antibodies.

Answer 72:

Bibliographic Information

Enhanced antitumor efficacy of cisplatin in combination with ALRT1057 (9-cis retinoic acid) in human oral squamous carcinoma xenografts in nude mice. Shalinsky, David R.; Bischoff, Eric D.; Gregory, Margaret L.; Lamph, William W.; Heyman, Richard A.; Hayes, J. Scott; Thomazy, Vilmos; Davies, Peter J. A. Departments Retinoid and Endocrine Research, Ligand Pharmaceuticals, Inc., San Diego, CA, USA. Clinical Cancer Research (1996), 2(3), 511-20. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 124:331989 AN 1996:208597 CAPLUS

Abstract

Cisplatin (DDP) is commonly used to treat head and neck tumors. Therapy frequently fails due to development of DDP resistance or toxicities assocd. with DDP therapy. In this study, effects of ALRT1057 [9-cis retinoic acid (9-cis RA)] on DDP cytotoxicity were studied in a human oral squamous carcinoma xenograft model. Mice bearing xenografts were dosed p.o. daily 5 days/wk with 30 mg/kg 9-cis RA and/or i.p. twice weekly with 0.3-0.9 mg/kg DDP. Max. tolerated doses of 9-cis RA and DDP were approx. 60 and ≥2.9 mg/kg, resp., under their dosing schedules and routes of administration. Control tumors grew rapidly with mean doubling times of 4 days and reached mean vols. of 1982 mm3 after 24 days. DDP at doses of 0.3, 0.45, and 0.9 mg/kg inhibited tumor growth by 28, 47, and 86%, resp., 24 days after tumor cell implantation. Thirty mg/kg 9-cis RA inhibited tumor growth by 25%. In combination, 0.3 mg/kg DDP + 30 mg/kg 9-cis RA inhibited tumor growth by 68%; 0.45 mg/kg DDP + 30 mg/kg 9-cis RA inhibited growth by 78%. These decreases were greater than those that would have been produced by either agent summed sep. Of importance, at doses of 9-cis RA that enhanced DDP cytotoxicity, no change in dose tolerance was obsd. as compared to tolerances obsd. for either agent alone, indicating that 9-cis RA increased sensitivity to DDP without altering systemic toxicity. In addn., 9-cis RA profoundly altered squamous cell carcinoma phenotypes by suppressing squamous cell differentiation, resulting in tumors with increased nos. of basal

cells. In contrast, DDP selectively depleted proliferating basal cells from carcinomas. In combination, morphol. changes produced by 9-cis RA alone predominated, suggesting a possible basis for enhanced DDP sensitivity in tumors exposed to both agents. These data demonstrate that 9-cis RA enhances tumor sensitivity to DDP, and suggest that this combination should be tested in Phase I-II clin. trials for its potential for improving anticancer therapy of squamous cell cancers.

Answer 73:

Bibliographic Information

Antitumor activity of cis-diamminedichloroplatinum(II) against human tumor xenografts depends on its area under the curve in nude mice. Kurihara, Naoto; Kubota, Tetsuro; Hoshiya, Yasunori; Otani, Yoshihide; Watanabe, Masahiko; Kumai, Koichiro; Kitajima, Masaki. School of Medicine, Keio University, Tokyo, Japan. Journal of Surgical Oncology (1996), 61(2), 138-42. Publisher: Wiley-Liss, CODEN: JSONAU ISSN: 0022-4790. Journal written in English. CAN 124:249895 AN 1996:169009 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A pharmacodynamic anal. of cis-diamminedichloroplatinum(II) (DDP) was conducted using two human gastric cancer xenografts, SC-1-NU and MKN-45, and one human breast cancer xenograft, MX-1, grown serially in BALB/c nu/nu mice. DDP was administered i.p. (i.p.) at a total dose of 5, 10, or 20 mg/kg in a schedule of q7d × 3 or (qd × 5) × 3. DDP was also administered i.p. to BALB/c +/ mice, whose plasma was used for the assay of total and free platinum by the at. absorption method. A total dose of 20 mg/kg DDP seemed to be the max. tolerated dose that was effective on MX-1 and SC-1-NU. When the totally administered doses were equiv., the antitumor effects of the q7d × 3 and (qd × 5) × 3 schedules were similar to each other. The antitumor activity of DDP against MKN-45 was dependent on the total administered dose as well as the area under the curve of free and total platinum in the plasma. Side effects were significantly reduced using a schedule of (qd × 5) × 3 in terms of body and spleen wt. loss when a total of 10 or 20 mg of DDP per kg was administered. These results suggest that DDP would be useful when administered using a daily schedule for obtaining the same antitumor activity as that of bolus injection but with reduced adverse effects.

Answer 74:

Bibliographic Information

Adding a reverser (verapamil) to combined chemotherapy overrides resistance in small cell lung cancer xenografts. Arvelo, F.; Poupon, M. F.; Bichat, F.; Grossin, F.; Bourgeois, Y.; Jacrot, M.; Bastian, G.; Le Chevalier, T. CNRS, Institut Curie, Paris, Fr. European Journal of Cancer, Part A (1995), 31A(11), 1862-8. Publisher: Elsevier, CODEN: EJCTEA Journal written in English. CAN 124:134977 AN 1996:39796 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Small cell lung carcinomas (SCLC) are characterized by chemosensitivity to diverse antitumoral compds. However, responses are transitory and relapses are commonly obsd. The authors examd. the ability of verapamil, a reverser of P-glycoprotein (Pgp)-related resistance, to improve the efficacy of CyCAV combined chemotherapy (Cy, cyclophosphamide (CPA); C, cisplatin (CDDP); A, doxorubicin (ADM);V, etoposide (VP16)), as currently administered to SCLC patients at Institute Gustave-Roussy, France, and adapted to the treatment of nude mice implanted with these tumors. Although Pgp encoded by the MDR1 (multidrug resistance) gene is not the only mechanism for multidrug resistance (MDR), and not all drugs included in this regimen are recognized by Pgp, the authors anticipated a therapeutic benefit. Four different SCLC lines, expressing the MDR1 gene and recently grafted into nude mice, were used. SCLC-75, SCLC-6 and SCLC-41 originated from untreated patients, and SCLC-74T was derived from a patient treated with a combination of ADM, CPA and VP16. SCLC-41T and SCLC-6T tumors were used after having undergone, resp., five and nine cycles of in vivo passage and CyCAV treatment of the tumor-bearing nude mice, to reinforce their chemoresistance. The efficacy of the CyCAV regimen, assocd. with or without verapamil (given 24 h before CyCAV on days 1-5), was tested on the growth of these SCLC. Verapamil (25 mg/kg) improved the antitumor effect of CyCAV in mice bearing SCLC-6T, SCLC-41T and SCLC-75 tumors, although toxicity was obsd. Verapamil modestly delayed the plasma clearance of ADM. Two daily injections of 10 mg/kg of verapamil,

administered at a 3 h interval, proved to be effective, whereas the same total dose administered as a bolus was not. These results indicate that the assocn. of some reversers of MDR, including drugs possibly interacting with Pgp, might potentiate SCLC combined chemotherapy.

Answer 75:

Bibliographic Information

Experimental regional hyperthermic chemotherapy on a human breast cancer xenograft (MX-1) serially transplanted into nude mice--combined effect of CDDP intralesional administration and local hyperthermia. Kobayashi, Koji. Tokyo Women's Medical College, Daini Hospital, Japan. Journal of Japan Society for Cancer Therapy (1995), 30(6), 830-40. Publisher: Nippon Gan Chiryo Gakkai, CODEN: NGCJAK ISSN: 0021-4671. Journal written in Japanese. CAN 123:246177 AN 1995:802490 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor effect of exptl. intralesional CDDP (cisplatin) administration combined with local hyperthermia (LH) was examd. Six-eight wk old nude mice underwent transplantation of human breast cancer MX-1 in the femoral root, and 3 wk later they were divided into three groups given CDDP intralesional administration alone, LH alone or a combination of both. The first group was given 5 CDDP intralesional doses to a total dose of 50, 25, 15 or 7.5mg/kg. The second group underwent local water bath therapy at 43° for 20 min once or twice a week, and the third group underwent LH (twice a week) immediately after CDDP intralesional administration (total dose, 15 mg/kg). Each tumor was resected at 3 wk to evaluate the antitumor effect. The tissue Po2 (Tpo2) was serially measured, and the platinum concn. (Pt) in the resected tumor was also detd. Intralesional administration of CDDP was effective when the total dose was 15 mg/kg or more. Plain LH suppressed tumor growth when given twice a week. The combination therapy showed a synergistic effect. There was no difference in the duration of decreased Tpo2 between the LH group and the combination therapy group. The Pt concn. in tumor tissue was about 1.7-fold higher in the combination therapy group than in the intralesional administration group, suggesting heat-accelerated distribution of the drug over the tumor tissue.

Answer 76:

Bibliographic Information

Complete inhibition of human ovarian cancer xenografts in nude mice by suramin and cis-diamminedichloroplatinum(II). Kikuchi, Yoshihiro; Hirata, Junko; Hisano, Atsushi; Tode, Takehiko; Kita, Tsunekazu; Nagata, Ichiro. Department Obstetrics and Gynecology, National Defense Medical College, Saitama, Japan. Gynecologic Oncology (1995), 58(1), 11-15. Publisher: Academic, CODEN: GYNOA3 ISSN: 0090-8258. Journal written in English. CAN 123:187869 AN 1995:727761 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

In this study, we have detd. the adjuvant effects of suramin to cis-diamminedichloroplatinum(II) (CDDP) on human ovarian cancer (KF) cell growth in vitro and in vivo. Suramin inhibited the ovarian cancer cell proliferation in vitro in a dose-dependent manner between 10 and 80 μM, showing the IC50 of 29 μM. From anal. of flow cytometry (FCM), suramin seemed to be a blocker of G2-M phase of the cell cycle. From the results of the isobologram, suramin appeared to have additive and somewhat synergistic effects on antitumor activity of CDDP. When 5×105 KF cells were inoculated s.c. into the right flank of nude mice, 8 of 10 mice formed solid tumor at 4 wk. When 2 mg/kg CDDP was administered i.p. every week, the 80% tumor formation was prolonged to 10 wk. Treatment with 5 and 10 mg/kg suramin decreased the formation rate of palpable tumor to 50 and 30%, resp. When CDDP was followed by 5 or 10 mg/kg suramin, the tumor formation rate was 20 or 0%. If suramin was followed by CDDP, the tumor formation was not obsd. in any mouse during the exptl. period. These results suggest that suramin may provide a new strategy for treatment of refractory ovarian carcinoma.

Answer 77:

Bibliographic Information

Evaluation of hyperbaric oxygen as a chemosensitizer in the treatment of epithelial ovarian cancer in xenografts in mice.
Alagoz, Turgut; Buller, Richard E.; Anderson, Barrie; Terrell, Kristina L.; Squatrito, Robert C.; Niemann, Theodore H.; Tatman, David J.; Jebson, Peter. Department of Obstetrics and Gynecology, University of Iowa Hospitals and Clinics, Iowa City, IA, USA.
Cancer (New York, NY, United States) (1995), 75(9), 2313-22. CODEN: CANCAR ISSN: 0008-543X. Journal written in English.
CAN 123:392 AN 1995:586968 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Resistance to chemotherapy is common in bulky hypoxic tumors such as epithelial ovarian cancer. Hyperbaric oxygen (HBO) oxygenates hypoxic tissues and promotes neovascularization. These unique properties of HBO may help overcome chemotherapy resistance by increasing both tumor perfusion and cellular sensitivity. This study was undertaken to det. if HBO increases the response of epithelial ovarian cancer to cisplatin chemotherapy. In Phase I, 64 nu/nu mice were divided into four groups and s.c. inoculated with cells from the A2780 human epithelial ovarian cancer cell line. Group 1 served as controls. Group 2 received weekly i.p. cisplatin (3.15 mg/kg). Group 3 was exposed to HBO (dives) at 2.4 atm abs. pressure for 90 min, 7 days a week. Group 4 received both cisplatin and HBO. In Phase II, 72 mice were divided into two groups and similarly inoculated. Both groups received weekly i.p. cisplatin (2.5 mg/kg). Group 1 was not exposed to HBO. Group 2 was exposed to HBO for 5 days a week. Dramatic tumor neovascularization was found in tumors of mice exposed to HBO. There was significant tumor growth retardation in Phase I for mice receiving both cisplatin and HBO compared with those treated with cisplatin alone. This significance was noted after just two doses of cisplatin but subsequently lost due to reduced nos. of mice. In Phase II, neovascularization was detectable after 10 HBO treatments (2 wk) and was maximal after 15 treatments (3 wk). Thus, hyperbaric oxygen increases vascularity in bulky tumors such as epithelial ovarian cancer. There appears to be a relation between increased vascularity and enhanced response to chemotherapy that merits further investigation.

Answer 78:

Bibliographic Information

Successful local regional therapy with topotecan of intraperitoneally growing human ovarian carcinoma xenografts.
Pratesi, G; Tortoreto, M; Corti, C; Giardini, R; Zunino, F. Divisions of Experimental Oncology B, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy. British Journal of Cancer (1995), 71(3), 525-8. CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 122:255667 AN 1995:484791 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The therapeutic effects of i.p. topotecan, a water-sol. camptothecin analog, were investigated in two models of human ovarian carcinoma xenografted i.p. into nude mice: the IGROV-1 tumor, which originated from an untreated patient, and the A2780 tumor, selected for resistance in vitro to cisplatin (A2780DDP). In IGROV-1 tumor-bearing mice, the optimal dose (10 mg kg-1) of topotecan, given i.p. every 4 days for four occasions markedly increased survival time over control mice (300 T/C%) and cured 4/9 mice, and such effects were not achieved by any of the clin. available drugs tested, i.e. cisplatin, carboplatin and doxorubicin delivered i.p. according to their optimal doses and schedules. In the treatment of A2780DDP tumor-bearing mice, topotecan was very effective since, at dose levels of 6.6 and 10 mg kg-1 every 4 days for four occasions, 15/18 mice survived more than 100 days, and most of them (12/15) were tumor free. The high responsiveness of this tumor to topotecan might be related to the elevated expression of the target enzyme topoisomerase I. From these results, i.p. treatment with topotecan appears to be a promising approach in the therapy of refractory ovarian cancer confined to the peritoneal cavity.

Answer 79:

Bibliographic Information

Synergistic antitumor activity of combination chemotherapy with mitomycin C and cisplatin against human gastric cancer xenografts in nude mice. Saikawa, Yoshiro; Kubota, Tetsuro; Kuo, Tsong-Hong; Furukawa, Toshiharu; Kase, Suguru; Tanino, Hirokazu; Isobe, Yo; Watanabe, Masahiko; Ishibiki, Kyuya; et al. School of Medicine, Keio University, Japan. Journal of Surgical Oncology (1994), 56(4), 242-5. CODEN: JSONAU ISSN: 0022-4790. Journal written in English. CAN 121:245426 AN 1994:645426 CAPLUS

Abstract

A new combined cancer chemotherapy regimen of mitomycin C (MMC) and cisplatin (DDP) showed synergistic antitumor activity against human gastric cancer xenografts St-40 and SC-1-NU in BALB/c nu/nu mice. The drugs were administered i.p. at doses of 2 or 4 mg/kg for MMC and 3 or 6 mg/kg for DDP, resp. To clarify the schedule-dependent antitumor activity of MMC and DDP against St-40 and SC-1-NU, different sequential therapies were conducted. Simultaneous administration of these agents showed the highest antitumor activity against SC1-NU among the three regimens used, whereas the sequence of MMC followed by DDP showed higher antitumor activity than the reverse sequence against St-40. The intratumoral concn. of platinum was significantly increased in St-40 treated with the sequence MMC to DDP, in comparison with the sequence DDP to MMC. The max. tolerated dose (MTD) of this combination was 4 mg MMC plus 6 mg DDP per kg in all the combinations, and these MTDs were 2/3 of the corresponding values for their single use. Since this combination increased the antitumor activity of each single agent without any increase in their toxicity, it would appear to be useful clin.

Answer 80:

Bibliographic Information

Predictability of clinical response to anticancer agents in human cancer xenografts. Tsukamoto, Fumine. Med. Sch., Osaka Univ., Suita, Japan. Osaka Daigaku Igaku Zasshi (1994), 46(4), 251-61. CODEN: ODIZAK ISSN: 0369-710X. Journal written in Japanese. CAN 121:124753 AN 1994:524753 CAPLUS

Abstract

Nude mouse transplanted human tumors retained original sensitivity to antitumor drugs, and was useful in secondary screening for the sensitivity to tumor chemotherapy. Fresh tumor tissues were transplanted and maintained in nude mice in 77 cases (tried: 247 cases), and sensitivity of the transplanted tumors to chemotherapy was compared between human therapy and in nude mice using regimen used clin. in 17 cases with 21 expts. (stomach, breast, colon, pancreas, esophagus. melanoma). Tested drugs were adriamycin, cisplatin, cyclophosphamide, cytarabine, dacarbazine, doxifluoridine, epirubicin, 5-fluorouracil, M-83 (a mitomycin C deriv.), mitomycin C, tegafur, and UFT. Chemotherapy in nude mice was effective in 6 expts., which coincided with clin. results in 5 cases. The ineffective 15 cases in nude mice coincided with the clin. results in all cases.

Answer 81:

Bibliographic Information

Local hyperthermia enhances cyclophosphamide, ifosfamide and cis-diamminedichloroplatinum cytotoxicity on human-derived breast carcinoma and sarcoma xenografts in nude mice. Wiedemann, Guenter; Roszinski, Stefan; Biersack, Anke; Weiss, Christoph; Wagner, Thomas. Dep. Intern. Med., Med. Univ. Luebeck, Luebeck, Germany. Journal of Cancer Research and Clinical Oncology (1992), 118(2), 129-35. CODEN: JCROD7 ISSN: 0171-5216. Journal written in English. CAN 120:153172 AN 1994:153172 CAPLUS

Abstract

Antitumor response and toxicity of locally applied hyperthermia with or without cyclophosphamide, ifosfamide, and cis-diamminedichloroplatinum (cisplatin) have been compared. The model systems were human breast carcinoma (MX1/3) and human

sarcoma (S117) grown in nude mice. To detect changes of tumor oxygenation, intratumoral PO2 and pH were measured before, during and following hyperthermia. In both human tumor lines, a monotherapy with one of the cytotoxic drugs or with hyperthermia caused a transient growth delay, while the combination of the same dose of the drugs with hyperthermia (at 43° for 1 h) resulted in complete tumor remissions. During hyperthermia, in both tumor types, oxygenation was improved. Intratumoral pH remained practically unchanged.

Answer 82:

Bibliographic Information

Antitumor activity of combination treatment of BOF-A2 with CDDP against human lung cancers xenografted in nude mice. Fujita, Fumiko; Fujita, Masahide; Sakamoto, Yasuo; Taguchi, Tetsuo. Exp. Cancer Chemother. Res. Lab., Co., Ltd., Osaka, Japan. Gan to Kagaku Ryoho (1993), 20(2), 215-21. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 119:424 AN 1993:400424 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

CDDP, commonly used in cancer chemotherapy, behaves as not only effector but also modulator of 5-FU when combined with 5-FU and its derivs. Therefore, the antitumor activity of combination treatment of BOF-A2, a new 5-fluorouracil deriv., with CDDP was evaluated with two human lung cancers (H-74 and LC-376) xenografted in nude mice. BOF-A2 was orally administered at 30 mg/kg (MTD) or 15 mg/kg (1/2 MTD) 3 times a week totally twelve times, and CDDP was administered i.p. at 5 mg/kg (MTD) or 2.5 mg/kg (1/2 MTD) once a week totally 4 times. The antitumor effect of combination of two drugs at the 1/2 MTD was effective to H-74 and markedly effective to LC-376, and the effect was more remarkable than each drug administered individually at the 1/2 MTD, and the combination effect was additive. The effect by the combination was not synergistic but showed a similar activity compared with single drug given individually at the MTD. Moreover, the side effect of combination of the 1/2 MTD was less than group given MTD of CDDP in terms of body wt. loss. These data suggests a clin. usefulness of combination BOF-A2 with CDDP against lung cancer.

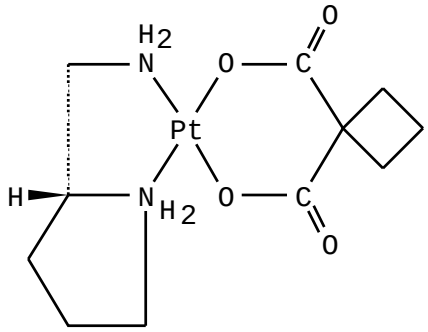
Answer 83:

Bibliographic Information

In vitro and in vivo antineoplastic activity of a new platinum antineoplastic agent, (R)-(-)-1,1-cyclobutanedicarboxylate (2-aminomethylpyrrolidine)platinum (II) (DWA2114R) on freshly separated human tumor cells and human tumor xenografts transplanted in nude mice - a comparison with cis-diamminedichloroplatinum (CDDP). Nio, Yoshinori; Imai, Shiro; Shiraishi, Takahiro; Tsubono, Michihiko; Morimoto, Hideki; Tseng, Chen Chiu; Tobe, Takayoshi. Fac. Med., Kyoto Univ., Kyoto, Japan. Anticancer Research (1991), 11(2), 761-7. CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 115:222883 AN 1991:622883 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The in vitro antimetabolic effect of a newly synthesized platinum antineoplastic agent, DWA2114R (I), on 72 fresh human tumors was compared with that of cis-platinum (CDDP). DWA2114R is reported to have a lower nephrotoxicity than CDDP, but is as strong an inhibitor of DNA synthesis as CDDP. In vitro IC50 was assessed in 10 tumors; the IC50 of DWA2114R ranged between 9.2 and 107 μM and that of CDDP ranged between 0.9 and 40 μM. DWA2114R had an antitumor spectrum similar to that of CDDP. Primary esophageal and pancreatic cancers were sensitive to DWA2114R, and cells sepd. from malignant effusion or metastatic lymph nodes were more sensitive than those from primary lesions. Nude mice were transplanted with 3 kinds of human tumor xenografts (esophageal, pancreatic and bile duct cancer lines), and were then treated with CDDP or DWA2114R at 4 times the clin. doses. CDDP significantly inhibited the growth of all the 3 lines, and DWA2114R inhibited the growth of 2 of the lines. The effect of DWA2114R on body wt. was smaller than that of CDDP. These results suggest that DWA2114R may be less potent than CDDP but may be useful as a new platinum antineoplastic agent with lower grade of side effects than CDDP.



I

Answer 84:

Bibliographic Information

Studies on chemotherapy for adenocarcinoma of the uterine cervix using xenografts transplanted in nude mice. Yamagishi, Masaji. Fac. Med., Toyama Med. Pharm. Univ., Toyama, Japan. Nippon Sanka Fujinka Gakkai Zasshi (1991), 43(2), 165-72. CODEN: NISFAY ISSN: 0300-9165. Journal written in Japanese. CAN 115:341 AN 1991:400341 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Adenocarcinoma of the human uterine cervix was successively transplanted into nude mice and the effects of chemotherapy on adenocarcinoma of uterine cervix were investigated in this transplanted tumor. First, it was confirmed that both the original tumor and the transplanted tumor were apparently histol. the same as adenocarcinoma of the uterine cervix (endocervical type). And the transplanted tumor was shown to have the features of adenocarcinoma by an electron microscope. The doubleing time of the transplanted tumor was 9.2 days. For the chemotherapy study, first the therapeutic effects of 11 kinds of agents were screened by single-agent chemotherapy applied to the transplanted tumor. From the results of this series, 6 regimens for multi-agent chemotherapy were tried on the transplanted tumor. The effects of the chemotherapy were evaluated following Battelle Columbus Labs. Protocol and histopathol. The relative regression rates for the tumors treated with mitomycin C (MMC) + cyclophosphamide (CPM) and MMC + CPM + methotrexate (MTX) were 72.99 and 80.9% (Tn/To = 0.84), resp. The results suggest that the combinations of MMC + CPM or MMC + CPM + MTX are regimens that are possibly effective on the adenocarcinoma of human uterine cervix and are worth be trying clin.

Answer 85:

Bibliographic Information

Effects of 5-FU and cis-DDP combination on human colorectal tumor xenografts. Pratesi, Graziella; Manzotti, Carla; Tortoreto, Monica; Prosperi, Ennio; Zunino, Franco. Div. Exp. Oncol. B, Ist. Naz. Stud. Cura Tumori, Milan, Italy. Tumori (1989), 75(1), 60-5. CODEN: TUMOAB ISSN: 0300-8916. Journal written in English. CAN 111:356 AN 1989:400356 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor effect against primary or metastatic human colorectal carcinoma xenografted in nude mice was better with cis-DDP (cisplatin) plus 5-Fu (5-fluorouracil) given i.v. at 24-h intervals than with either drug alone; lower drug doses were tolerated by using cisplatin-5-FU sequence.

Answer 86:

Bibliographic Information

Combined effects of UFT with other anticancer agents using in vivo chemosensitivity tests. Nishiyama, Masahiko; Niimi, Ken; Takagami, Shinichi; Hirabayashi, Naoki; Yamaguchi, Masahiro; Saeki, Toshiaki; Yoshinaka, Ken; Dian-Chang, Wang; Niimoto, Minoru; Hattori, Takao. Res. Inst. Nucl. Med. Biol., Hiroshima Univ., Hiroshima, Japan. Japanese Journal of Surgery (1988), 18(1), 93-7. CODEN: JJSGAY ISSN: 0047-1909. Journal written in English. CAN 109:389 AN 1988:400389 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The combined and tumor activity of UFT (tegafur-uracil mixt. 1:4 molar ratio) and other anticancer agents (mitomycin C, 5-fluorouracil, adriamycin, methotrexate, and cis-diamminedichloroplatinum) were studied against 3 human tumor xenografts in a nude mouse exptl. system and in a subrenal capsule assay. The effectiveness of the combination of UFT and mitomycin C was shown in both assays against all tumor xenografts tested.

Answer 87:

Bibliographic Information

A new experimental metastasis model in athymic nude mice, the human malignant melanoma LOX. Fodstad, Oystein; Aamdal, Steinar; McMenamin, Mary; Nesland, Jahn M.; Pihl, Alexander. Inst. Cancer Res., Norwegian Radium Hosp., Oslo, Norway. International Journal of Cancer (1988), 41(3), 442-9. CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 108:179729 AN 1988:179729 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The human tumor line LOX was established as an s.c. xenograft in nude mice from a lymph-node metastasis of patient with malignant melanoma. I.v. injection into adult nude mice of single-cell suspensions prepd. from xenografts resulted in progressively growing lung tumor colonies that killed the animals. No difference in colony formation was seen between cells taken from lung colonies and s.c. xenografts. An in vitro cell line, LOX-L, was established from lung colonies, and the monolayer cells, detached with EDTA, retained the same ability to form exptl. lung metastases. N a total of 14 expts., 82 of 89 mice receiving 1 × 106 viable tumor cells died with a mean survival time of 34.1 days. Long-term passaging in vivo and in vitro did not result in any alteration of the lung-colonizing potential of the LOX cells. whereas trypsinization of the cells before i.v. injection reduced lung colony formation. The life span was inversely related to the no. of LOX cells injected, permitting estn. of the cell kill caused by chemotherapy. Mice injected i.v. with the LOX cells showed the same relative response to cis-diamminedichloroplatinum and mitozolomide as did animals carrying s.c. xenografts. The LOX cells have shown a remarkable stability and similarity to the cells of the patient's tumor with resp. to morphol., karyotype and chemosensitivity. The LOX model may be useful or testing effects of therapy on lung micro- and macrometastases, and the activity of antimetastatic agents, as well as for studying mechanisms involved in the metastatic process.

Answer 88:

Bibliographic Information

Augmentation of activity of cis-diamminedichloroplatinum(II) and mitomycin C by interferon in human malignant mesothelioma xenografts in nude mice. Sklarin, Nancy T.; Chahinian, A. Philippe; Feuer, Eric J.; Lahman, Liz A.; Szrajer, L.; Holland, James F. Mt. Sinai Sch. Med., City Univ. New York, New York, NY, USA. Cancer Research (1988), 48(1), 64-7. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 108:48895 AN 1988:48895 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Two human mesothelioma xenograft lines, BG and ES, serially passaged in athymic mice, were studied to det. the efficacy of α-interferon in this type of tumor. Treatment began after progressive tumor growth was established. Recombinant human α-interferon-2a (Roferon-A) was given s.c. at a site distant from the tumor, at a dose of 2 × 105 IU 5 days per wk for 5 wk. Mild inhibitory activity was noted in both lines with interferon alone. cis-Diamminedichloroplatinum(II) (CDDP) (4 mg/kg) weekly × 5 was effective in line BG, while mitomycin C (1.5 mg/kg) weekly × 3 was effective in line ES. CDDP was not as effective in line ES. The moderate activity of CDDP in line BG and of mitomycin C in line ES was markedly increased by the addn. of α-interferon. The combination of mitomycin C and α-interferon was as effective as mitomycin C and CDDP. No addnl. toxicity was noted by the addn. of α-interferon. The combination of recombinant human α-interferon-2a and active chemotherapeutic agents is effective in mesothelioma xenografts.

Answer 89:

Bibliographic Information

Fundamental and clinical investigations on the reinforcement of the effects of combination cancer chemotherapy by flow cytometric analysis of DNA histograms. New attempts at reinforcement of antitumor effects using FCM. Sato, Yasumitsu. Sch. Med., Akita Univ., Japan. Akita Igaku (1986), 13(4), 561-86. CODEN: AKIGDV ISSN: 0386-6106. Journal written in Japanese. CAN 107:168379 AN 1987:568379 CAPLUS

Abstract

The effects of cis-diamminedichloroplatinum (CDDP), peplomycin (PEP), mitomycin C (MMC), adriamycin (ADM), etoposide (VP-16), 5-fluorouracil (5-FU), and vindesine (VDS) upon the viability and cell cycle progression of cultured human esophageal cancer cells (TE-2, AE-2), human esophageal (AEN-2), or gastric (TK) tumor xenografts growing in nude mice were measured and compared using flow cytometry (FCM) in order to improve the methods of selecting the individual agents and establish the most effective regimen for combination cancer chemotherapy. Anal. of the influence of chemotherapeutic agents on cell cycle kinetics using FCM appeared to be very important in the development of an effective cancer chemotherapy. Recruitment and partial synchronization were esp. useful in reinforcing the antitumor effects of combination chemotherapy on solid cancers.

Answer 90:

Bibliographic Information

Effects of alternating chemotherapy with 2 non-cross-resistant drug combinations on human alimentary and breast cancer xenografts in nude mice. Fujita, Fumiko; Fujita, Masahide; Yamauchi, Teruo; Sakamoto, Yasuo; Shimozuma, Kojiro; Inaba, Hiizu; Taguchi, Tetsuo. Res. Inst. Microb. Dis., Osaka Univ., Osaka, Japan. Gan to Kagaku Ryoho (1987), 14(5, Pt. 1), 1297-304. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 107:126598 AN 1987:526598 CAPLUS

Abstract

The effectiveness of alternating chemotherapy with the combination regimens I [mitomycin C (MMC) and 5'-deoxy-5-fluorouridine (5'-DFUR)] and II [cisplatin(CDDP), 5'-DFUR, and vindesine(VDS)] was evaluated using 3 lines of cancer xenografts (breast, colon, and pancreas) in nude mice with special emphasis on relapse-free survival. Results showed that cyclic delivery of two non-cross-resistant drug combinations with optimal treatment doses and timing prevented toxic effects and induced long-term survival without relapse.

Answer 91:

Bibliographic Information

Sensitivity of human non-small cell lung cancer xenografts to cyclophosphamide and cisplatin. Mattern, J.; Wayss, K.; Volm, M. Inst. Exp. Pathol., Ger. Cancer Res. Cent., Heidelberg, Fed. Rep. Ger. In Vivo (1987), 1(1), 23-6. CODEN: IVIVE4 ISSN: 0258-851X. Journal written in English. CAN 107:126374 AN 1987:526374 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor activity of cyclophosphamide and cisplatin was tested against 14 human non-small cell lung tumor xenografts in nude mice. The previously reported poor clin. response of non-small cell tumors to these 2 drugs paralleled the lack of response of the xenografts. Thus, the nude mouse xenograft system may be used as a predictive screen for antineoplastic agents.

Answer 92:

Bibliographic Information

Comparative antitumor activity of cisplatin and two new cisplatin-analogs JM8 and JM9 in human testicular carcinoma xenografts. Harstrick, A.; Casper, J.; Schmoll. H. J. Abt. Haematol. Onkol., Med. Hochsch. Hannover, Hannover, Fed. Rep. Ger. International Journal of Andrology (1987), 10(1), 139-45. CODEN: IJANDP ISSN: 0105-6263. Journal written in English. CAN 107:70346 AN 1987:470346 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The comparative antitumor activity of cisplatin, JM8 and JM9 was tested using a panel of different heterotransplanted human testicular tumor cell lines. All drugs were applied at equitoxic doses in a 5 day schedule. In the two cisplatin sensitive cell lines 2102 EP and H 12.1 both analogs were inferior to cisplatin. No significant therapeutic effect was achieved with any of the three drugs in the cisplatin resistant line H 23.1. Thus JM8 and JM9 seem to be less active in cisplatin sensitive tumors and seem to be of no advantage in the case of cisplatin resistance.

Answer 93:

Bibliographic Information

In vivo cell kinetic effects of cis-platinum on human ovarian cancer xenografts measured by dual parameter flow cytometry. Sevin, Bernd Uwe; Pollack, Alan; Averette, Hervy E.; Ramos, Reinaldo; Donato, Daniel. Sch. Med., Univ. Miami, Miami, FL, USA. Cytometry (1987), 8(2), 153-62. CODEN: CYTODQ ISSN: 0196-4763. Journal written in English. CAN 107:17353 AN 1987:417353 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Human ovarian cancer xenografts in nude mice from a primary and recurrent tumor of the same patient were studied. The response to i.p. application of cis-platinum was assessed by tumor vol. measurements, changes in labeling indexes by autoradiog., and dual parameter flow cytometry. Pretherapy samples were compared to multiple specimens collected up to 18 days after therapy. Morphol. changes of each specimen were also assessed. cis-Platinum affects malignant cells in the G1B, S, G2A, and G2B compartments with various intensities and different time frames, depending on the drug sensitivity of each individual tumor.

Answer 94:

Bibliographic Information

Chemo-sensitive differences of primary, metastatic and recurrent tumors of human colorectal cancer. Yamada, Kazutaka;

Takao, Sonshin; Maenohara, Shigeho; Saihara, Tetushi; Yoshinaga, Atsunori; Haruyama, Katsuro; Mitsuda, Kazunobu; Makizumi, Kanro; Ishizawa, Takashi; Shimazu, Hisaaki. Sch. Med., Kagoshima Univ., Kagoshima, Japan. Nippon Shokakibyo Gakkai Zasshi (1986), 83(11), 2318-24. CODEN: NIPAA4 ISSN: 0369-4259. Journal written in Japanese. CAN 106:207311 AN 1987:207311 CAPLUS

Abstract

Tumor lines xenografts in nude mice used in this study include COK-1 and COK-7. COK-1 (PT, LN and RE) has been established from the primary (PT) lymph node metastatic (LN) and local recurrent (RE) tumors of human colon cancer, and COK-7 (PT and LiM) has been established from the primary(PT) and liver metastatic(LiM) tumors of human rectal cancer. These tumor lines were used for the study of chemotherapeutic responses to such anti-cancer drugs as 5-fluorouracil [51-21-8], cyclophosphamide [50-18-0], cisplatin [15663-27-1], and mitomycin C (MMC) [50-07-7]. Chemotherapeutic responses to these drugs in each tumor line were as follows: COK-1 (PT) responded to only MMC, while COK-1 (RE) responded to both MMC and cisplatin. However, COK-1 (LN) did not respond to any drug studied. In case of COK-7 (PT) it did not respond to drug as well, though COK-7 (LiM) showed a response to MMC. These results indicate that each tumor line of COK-1 and COK-7 has chemosensitive differences in primary, metastatic, and recurrent tumor lines.

Answer 95:

Bibliographic Information

Efficacy of anticancer agents in vitro and in vivo using cultured human endometrial carcinoma cells. Study of therapeutic index. Yasui, Yoshie. Sch. Med., Nagoya City Univ., Nagoya, Japan. Nippon Sanka Fujinka Gakkai Zasshi (1987), 39(2), 303-6. CODEN: NISFAY ISSN: 0300-9165. Journal written in English. CAN 106:188338 AN 1987:188338 CAPLUS

Abstract

Employing the new cell line, NUE-1, which was derived from cells of ascites in a woman with endometrial carcinoma, the sensitivity test for anticancer agents was carried out in culture and xenografts in nude mice. Anticancer activity in vitro was evaluated by counting surviving cells, and the therapeutic index was expressed by LD50 for mice/MLD90 (90% mean LD) in vitro. NUE-1 cells were inoculated s.c. in BALB/c nude mice, and then tumors serially transplanted were used as materials. Anticancer agents (adriamycin (ADM) [23214-92-8], cisplatinum [15663-27-1], chromomycin A3 [7059-24-7], carbazilquinone [24279-91-2], and mitomycin C [50-07-7]) at 1/3 LD50 dosage for mice were administered i.p. on a schedule of 3 doses for every 4 days. The results were as follows: (a) the therapeutic index of ADM was highest at 5-19 times the others; (b) in vivo, ADM demonstrated chemotherapeutic effectiveness, whereas the others had no significant effect; and (c) there was a close correlation between the therapeutic index and in vivo anticancer effect using nude mice.

Answer 96:

Bibliographic Information

Monitoring by α-hydroxybutyrate dehydrogenase of human ovarian carcinoma grown in nude mice. Kikuchi, Yoshihiro; Miyauchi, Munenori; Oomori, Keibun; Kizawa, Isao; Kita, Tsunekazu; Seki, Katsuyoshi; Kato, Koichi. Dep. Obstet. Gynecol., Natl. Def. Med. Coll., Saitama, Japan. Journal of Cancer Research and Clinical Oncology (1986), 112(1), 19-22. CODEN: JCROD7 ISSN: 0171-5216. Journal written in English. CAN 105:112946 AN 1986:512946 CAPLUS

Abstract

To establish that the tumor burden in nude mice bearing a xenografted human ovarian tumor can be assessed by measuring plasma

levels of α-hydroxybutyrate dehydrogenase (HBD) (E.C. 1.1.1.30), the plasma HBD and the tumor vol. were measured every week after inoculation of a human ovarian carcinoma cell line designated HR. About 3 wk after tumor inoculation, all nude mice had a palpable tumor while elevated levels of HBD were obsd. in a half of the mice at that time. Thereafter the HBD levels rose with increasing tumor vol. There was a quant. linear relationship between the tumor wt. and HBD activity per mouse. When 40 μg of cisplatin (about 2 mg/kg) was administered i.p. every week for 5 wk 2 wk after inoculation, plasma levels of HBD were decreased on day 27 compared to those in untreated nude mice. Decreases in the HBD levels during treatment with cisplatin occurred 7 days prior to changes in tumor vols. Further, removal of local tumor mass resulted in a marked decrease in HBD levels on day 1 after surgery and the HBD levels in nude mice which had no recurrent tumor fell into the normal range 8 days after surgery.

Answer 97:

Bibliographic Information

Xenografts in pharmacologically immunosuppressed mice as a model to test the chemotherapeutic sensitivity of human tumors. Floersheim, G. L.; Bieri, A.; Chiodetti, Nicole. Zent. Lehre Forsch., Kantonssp., Basel, Switz. International Journal of Cancer (1986), 37(1), 109-14. CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 104:81665 AN 1986:81665 CAPLUS

Abstract

A human tumor xenograft model using pharmacol. immunosuppressed mice was assessed for its suitability to test preclinically the sensitivity of colorectal carcinomas, bone sarcomas and melanomas against anticancer agents. Beside ionizing radiation, 14 cytotoxic drugs including 5-fluorouracil (5-FU) [51-21-8], dimethylmyleran (DMM) [55-93-6], cytosine arabinoside [147-94-4], cyclophosphamide [50-18-0], melphalan [148-82-3], mitomycin C [50-07-7], adriamycin [23214-92-8], bleomycin [11056-06-7], etoposide [33419-42-0], vinblastine [865-21-4], cisplatin [15663-27-1], procarbazine [671-16-9], DTIC [4342-03-4], and BCNU [154-93-8] were assayed. Ionizing radiation, 5-FU and DMM were also applied at LDs followed by bone-marrow rescue high-dose therapy. Four colon carcinomas responded poorly to most of the agents but one tumor displayed marked sensitivity to BCNU. LDs of radiation, 5-FU and DMM and cyclophosphamide and by an osteosarcoma to the latter drug. No strong effects were seen against melanomas. LDs of DMM induced the best regression of one colon carcinoma. In general, the superiority of high-dose therapy for solid human tumors compared to maximally tolerated doses was demonstrated. Individual carcinomas of the same type displayed different drug sensitivity.

Answer 98:

Bibliographic Information

Secondary screening of platinum compounds in human ovarian cancer xenografts in nude mice. Boven, E.; Nauta, M. M.; Schluper, H. M. M.; Elferink, F.; Van der Vijgh, W. J. F.; Pinedo, H. M. Dep. Oncol., Free Univ. Hosp., Amsterdam, Neth. European Journal of Cancer & Clinical Oncology (1985), 21(10), 1253-60. CODEN: EJCODS ISSN: 0277-5379. Journal written in English. CAN 104:14636 AN 1986:14636 CAPLUS

Abstract

Five TNO Pt compds. were evaluated for antitumor activities in 2 human ovarian carcinoma tumor lines grown in nude mice. The most active drug, TNO-38 [91992-30-2], was investigated in 5 addnl. lines with a known range of sensitivity to cisplatin [15663-27-1]. None of the new compds. showed superior activity to cisplatin. The slightly lower activity of TNO-38 as compared to the parent compd. was reproducible in all tumor lines. Besides the similarity in the antitumor activity, a remarkably correspondence in Pt distribution and retention at 24 h of TNO-38 and cisplatin could be obsd. Chromatog. anal. of the compds. in their injection fluids showed single peaks for TNO-26 [99544-95-3] and TNO-38. The degrdn. products of the latter drugs may have affected their activity and toxicity. These human ovarian cancer xenografts may offer a reliable screening model for selection of a cisplatin analog with a higher therapeutic index or without cross-resistance for treatment in ovarian cancer.

Answer 99:

Bibliographic Information

Cytotoxicity of cisplatin and cisdiammine-1,1-cyclobutane dicarboxylate in MGH-U1 cells grown as monolayers, spheroids, and xenografts. Erlichman, Charles; Vidgen, Danka; Wu, Anna. Ontario Cancer Inst., Univ. Toronto, Toronto, ON, Can. JNCI, Journal of the National Cancer Institute (1985), 75(3), 499-505. CODEN: JJIND8 ISSN: 0198-0157. Journal written in English. CAN 103:153566 AN 1985:553566 CAPLUS

Abstract

The cytotoxicity of cisplatin [15663-27-1] and cis-diammine-1,1-cyclobutanedicarboxylate (CBDCA) [41575-94-4] was examd. using the MGH-U1 human bladder carcinoma cell line, grown as monolayer cultures, multicellular tumor spheroid(s) (MTS), and xenografts in immune-deprived CBA/CaJ mice. The cell survival of exponentially growing monolayers and MTS treated with cisplatin declined in a monoexponential fashion with a concn. of drug resulting in 10% colony survival (D10) of 7.75 μg/mL and 9.5 μg/mL, resp. MTS growth delay detn. demonstrated a drug concn.-dependent increase in growth delay and a correlation between decreasing surviving fraction and increasing growth delay. In vivo treatment of MGH-U1 xenografts with cisplatin caused a modest decrease in surviving fraction although the xenografted cells treated in vivo demonstrated the same sensitivity to cisplatin as those cells maintained continuously in vitro. The D10 for CBDCA treatment was 246 μg/mL for exponentially growing monolayer cells and 196 μg/mL for MTS. Growth-delay studies with CBDCA showed a concn.-dependent increase in spheroid growth delay and a correlation between decreasing surviving fraction and growth-delay similar to those with cisplatin. The conclusions were that: 1) cisplatin and CBDCA do not have any difficulty penetrating into spheroids, 2) both agents appear to be active against the noncycling poorly nourished cells found near the necrotic center of spheroids 3) both cisplatin and CBDCA are cytotoxic toward MGH-U1 cells but cisplatin is .apprx.20-30 times more effective, and 4) the limited cytotoxic effect of cisplatin in vivo may be due to the low area under the concn.-time curve achieved in vivo and not due to intrinsic cell resistance.

Answer 100:

Bibliographic Information

Activity of titanocene dihalides against a human colon carcinoma heterotransplanted to athymic mice. Koepf-Maier, P.; Moormann, A.; Koepf, H. Abt. Anat., Univ. Ulm, Ulm, Fed. Rep. Ger. European Journal of Cancer & Clinical Oncology (1985), 21(7), 853-7. CODEN: EJCODS ISSN: 0277-5379. Journal written in English. CAN 103:153498 AN 1985:553498 CAPLUS

Abstract

The antitumor activity of cis-diamminedichloroplatinum(II) and of 2 metallocene derivs., titanocene dichloride (C5H5TiCl2) [1271-19-8] and titanocene dibromide (C5H5TiBr2) [1293-73-8] was investigated against a human colon adenocarcinoma heterotransplanted to athymic mice. Whereas cis-diamminedichloroplatinum(II) induced an only marginal tumor-inhibiting effect, both titanocenes markedly suppressed tumor development and caused stagnation and relative decrease of tumor growth, when they were applied in subtoxic doses far below the LD10 level. The results are remarkable with respect to the general insensitivity of human colorectal carcinomas to cytostatic agents.

Answer 101:

Bibliographic Information

Possible relationship of chromosome abnormalities and gene amplification with effects of chemotherapy: a neuroblastoma xenograft study. Tsuchida, Yoshiaki; Kaneko, Yasuhiko; Kanda, Naotoshi; Makino, Shunichi; Utakoji, Tadashi; Saito, Sumio. Dep. Pediatr. Surg., Univ. Tokyo, Tokyo, Japan. Progress in Clinical and Biological Research (1985), 175(Adv. Neuroblastoma Res.), 171-80. CODEN: PCBRD2 ISSN: 0361-7742. Journal written in English. CAN 102:160157 AN 1985:160157 CAPLUS

Abstract

Human neuroblastoma xenografts (in nude mice) with extrachromosomal double minutes, but not homogeneously staining regions, were sensitive to the antitumor effects of aclacinomycin A [57576-44-0]; cisplatin [15663-27-1] was effective against neuroblastomas with abnormal chromosome 1. There was no correlation between amplification of a 1.75-kilobase homogeneous-staining region clone and chemotherapy. These observations are discussed with respect tp the role of chromosomal aberrations in drug resistance and tumor chemotherapy.

Answer 102:

Bibliographic Information

Fundamental studies on combination chemotherapy of cisplatin with peplomycin against human squamous cell carcinomas in nude mice. Ekimoto, Hisao; Aikawa, Minako; Takahashi, Katsutoshi; Matsuda, Akira. Res. Lab., Nippon Kayaku Co., Tokyo, Japan. Gan to Kagaku Ryoho (1985), 12(1), 70-6. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 102:142853 AN 1985:142853 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Combination chemotherapy of 5 human squamous cell carcinomas, xenografted in nude mice, with cisplatin [15663-27-1] and peplomycin [68247-85-8] was more effective when the Pt compd. was given before peplomycin; this effect was esp. marked when cisplatin was administered 5 or 3 days before the other drug. Human tumors transplanted in nude mice should be useful models in combination chemotherapy studies.

Answer 103:

Bibliographic Information

Comparative activity and distribution studies of five platinum analogs in nude mice bearing human ovarian carcinoma xenografts. Boven, Epie; Van der Vijgh, Wim J. F.; Nauta, Maria M.; Schluper, Hennie M. M.; Pinedo, Herbert M. Dep. Oncol., Free Univ. Hosp., Amsterdam, Neth. Cancer Research (1985), 45(1), 86-90. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 102:105827 AN 1985:105827 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor activity of 4 new Pt analogs was compared at equitoxic doses to that of cisplatin [15663-27-1] in B10 LP/cpb nude mice bearing xenografts of human ovarian carcinomas. The 2 tumor lines used, MRI-H-207 and Pe, differ in histol., tumor doubling time, and sensitivity to cisplatin. Complete remission of MRI-H-207 was obsd. with cisplatin, carboplatin [41575-94-4], iproplatin [62928-11-4], and JM-40 [41666-77-7] while spiroplatin [74790-08-2] only gave growth delay. Cisplatin and carboplatin caused some growth delay of Pe, while JM-40, spiroplatin, and iproplatin failed to affect tumor growth. Pr tissue distribution was also measured for each compd. in groups of 5 to 7 tumor-bearing mice. Pt concns. in the 2 tumors at 24 h were similar for cisplatin and carboplatin, but differed for iproplatin, spiroplatin, and JM-40. Organ distribution was similar for each analog, and concns. were significantly higher in kidneys than in liver, except for iproplatin with comparable concns. in these organs. These findings show a good correlation between analog activity in ovarian cancer in the clinic and that in MRI-H-207. Pt concns. in tumor tissue did not predict antitumor activity.

Answer 104:

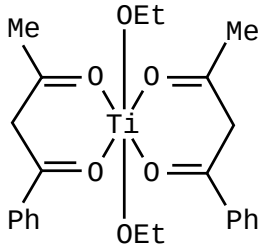
Bibliographic Information

Preclinical evaluation of diethoxy(1-phenyl-1,3-butanedionato)titanium(IV) in human tumor xenografts. Mattern, J.; Keppler, B.; Volm, M. Inst. Exp. Pathol., Dtsch. Krebsforschungszent., Heidelberg, Fed. Rep. Ger. Arzneimittel-Forschung (1984),

34(10), 1289-90. CODEN: ARZNAD ISSN: 0004-4172. Journal written in English. CAN 102:55764 AN 1985:55764 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor activity of diethoxy(1-phenyl-1,3-butanedionato)titanium(IV) (I) [85969-07-9] in comparison to cisplatin (cis-DDP) [15663-27-1] and cyclophosphamide (CTX) [50-18-0] against human breast, colorectal, and lung tumor lines growing as xenografts in nude mice was investigated. The antitumor activities and toxicities of I and cis-DDP were comparable, whereas CTX was the most effective agent.



I

Answer 105:

Bibliographic Information

Drug testing using a soft agar stem cell assay on patient and xenograft tumor material. Hanson, Jane; Coombs, Annie; Moore, John L. Radiobiol. Dep., Velindre Hosp., Whitchurch/Cardiff, UK. International Journal of Radiation Oncology, Biology, Physics (1984), 10(9), 1697-701. CODEN: IOBPD3 ISSN: 0360-3016. Journal written in English. CAN 102:17003 AN 1985:17003 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Fifty tumor samples from 10 different sites were studied. Over half were breast or ovarian tumors. Of the 27 that were considered suitable for cloning, 11 produced colony formation and 6 of these were drug tested. One ovarian granulosa cell tumor and its mouse xenograft (V7) were tested against several cytotoxic agents. During a period of 16 mo, sensitivity to cisplatin [15663-27-1] was relatively stable but sensitivity to vinblastine [865-21-4] was markedly changed when the original tumor cells and original cells stored in liq. N were compared with xenograft cells. These changes may be related to patient treatments prior to tumor sample collection. Gross histol. of original tumor and xenograft were similar. Chemosensitization in vivo of a breast xenograft (Hx99) to melphalan [148-82-3] by misonidazole [13551-87-6] was investigated. Misonidazole at a total dose of 0.5 g/kg given prior to melphalan (14 mg/kg) was an effective chemosensitizer.

Answer 106:

Bibliographic Information

Cell survival in four ovarian carcinoma xenografts following in vitro exposure to melphalan, cisplatin and cis-diammine-1,1-cyclobutanedicarboxylateplatinum(II) (CBDCA, JM8). Jones, Adrian C.; Wilson, Patricia A.; Steel, G. Gordon. Radiother. Res. Unit, Inst. Cancer Res., Sutton, UK. Cancer Chemotherapy and Pharmacology (1984), 13(2), 109-13. CODEN: CCPHDZ ISSN: 0344-5704. Journal written in English. CAN 101:183580 AN 1984:583580 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Four human ovarian carcinoma xenografts were established and maintained in immune-suppressed mice. Cells obtained from these xenografts were exposed in vitro to melphalan [148-82-3], JM8 [41575-94-4], and cisplatin [15663-27-1]; cell survival following a 1-h exposure was measured using a soft-agar colony assay. A similar dose-response curve was obtained with melphalan for each of the 4 xenografts, despite previous treatment with an alkylating agent in two of the patients from whom the xenografts originated. Cell survival was also compared after JM8 and cisplatin exposure in each individual xenograft. It was found to be similar for each tumor when the concns. of JM8 used were 10-fold greater than those of cisplatin. Early clin. studies in which JM8 has been shown to be effective in the treatment of ovarian carcinoma support the view that xenograft tumors may have a role in phase-II screening of new cytotoxic agents.

Answer 107:

Bibliographic Information

Increased cytotoxic effects of various anticancer drugs by α-interferon (HLBI) on human tumor xenografts in nude mice. Nosoh, Yoshihiro; Yoshinaka, Ken; Yamaguchi, Masahiro; Tani, Tadanori; Toge, Tetsuya; Niimoto, Minoru; Hattori, Takao. Res. Inst. Nucl. Med. Biol., Hiroshima Univ., Hiroshima, Japan. Gan to Kagaku Ryoho (1984), 11(8), 1623-8. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 101:163319 AN 1984:563319 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effect of 7 anticancer agents in combination with interferon on gastric cancer and malignant melanoma of human transplanted s.c. in nude mice was studied. Of the 7 drugs, mitomycin C [50-07-7] and adriamycin [23214-92-8] showed the greatest inhibition of tumor growth in combination with interferon.

Answer 108:

Bibliographic Information

Childhood rhabdomyosarcoma xenografts: responses to DNA-interacting agents and agents used in current clinical therapy. Houghton, Janet A.; Cook, Ruby L.; Lutz, Pamela J.; Houghton, Peter J. Div. Biochem. Clin. Pharmacol., St. Jude Child. Res. Hosp., Memphis, TN, USA. European Journal of Cancer & Clinical Oncology (1984), 20(7), 955-60. CODEN: EJCODS ISSN: 0277-5379. Journal written in English. CAN 101:163109 AN 1984:563109 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A lab. model of childhood rhabdomyosarcoma (RMS) has been used to evaluate cytotoxic agents used in current clin. protocols, and DNA-reacting agents that have had either limited or no evaluation in this histiotype. Seven lines of RMS each derived from a different patient were grown as xenografts in immune-deprived mice, six of these being from specimens derived from previously untreated patients. Of the conventional' agents, vincristine [57-22-7] was the most effective. Of the other agents evaluated [L-phenylalanine mustard (L-PAM) [148-82-3], cis-dichlorodiammineplatinum (cis-DDP) [15663-27-1], mitomycin C [50-07-7] and 5-(3,3-dimethyl-1-triazeno)-imidazole-4-carboxamide (DTIC) [4342-03-4]], L-PAM caused complete regressions in six of seven lines, including those resistant to cyclophosphamide [50-18-0]. DTIC had marked activity in five tumors, and mitomycin C in three lines. Cyclophosphamide was active in five tumors, although efficacy was less marked in two lines in comparison to DTIC and mitomycin C.

Answer 109:

Bibliographic Information

Effect of five antineoplastic agents on tumor xenografts with different growth rates. Mattern, Juergen; Wayss, Klaus; Volm,

Manfred. Dep. Exp. Pathol., German Cancer Res. Cent., Heidelberg, Fed. Rep. Ger. JNCI, Journal of the National Cancer Institute (1984), 72(6), 1335-9. CODEN: JJIND8 ISSN: 0198-0157. Journal written in English. CAN 101:103754 AN 1984:503754 CAPLUS

Abstract

The effects of cyclophosphamide (Cy) [50-18-0], doxorubicin (Dx) [23214-92-8], cisplatin (DDP) [15663-27-1], melphalan (L-PAM) [148-82-3], and vincristine (VCR) [57-22-7] on various human and animal tumor lines with different growth rates, growing as xenografts in NMRI (nu/nu) mice, were studied. Two types of response were obsd.: For Cy and Dx, the response of the xenografts was neg. correlated with tumor vol. doubling time (TD), indicating that rapidly growing tumors were more sensitive to these drugs than were slowly growing tumors. For DDP, L-PAM, and VCR, the effects were pos. correlated with the TD, indicating that slowly growing tumors were more sensitive to these drugs than rapidly growing tumors. The data are discussed in relation to the effects of the drugs on proliferating and nonproliferating cells obtained with other cell lines.

Answer 110:

Bibliographic Information

Renal cell carcinoma - xenotransplantation into immuno-suppressed mice. Kopper, L.; Magyarosy, E.; Nagy, P.; Lapis, K.; Szamel, I.; Eckhardt, S.; Csata, S.; Wabrosch, G.; Repassy, D. 1st Inst. Pathol. Exp. Cancer Res., Semmelweis Med. Univ., Budapest, Hung. Oncology (1984), 41(1), 19-24. CODEN: ONCOBS ISSN: 0030-2414. Journal written in English. CAN 100:150726 AN 1984:150726 CAPLUS

Abstract

Twenty one human renal cell carcinomas (RCC) were xenotransplanted into artificially immunosuppressed mice. Four tumors grew successfully retaining some characteristics of the primary tumors (according to morphol. and karyotype anal.), but losing metastatic capacity. One of the serially transplantable tumors (HT 40) with hyperdiploid cellular DNA content and estrogen receptor positivity failed to respond to the single maximally tolerated dose of several cytotoxic agents.

Answer 111:

Bibliographic Information

Calcitonin as an indicator of the response of human small cell carcinoma of the lung cells to drugs and radiation. Cate, Charles C.; Douple, Evan B.; Andrews, Kim M.; Pettengill, Olive S.; Curphey, Thomas J.; Sorenson, George D.; Maurer, L. Herbert. Norris Cotton Cancer Cent., Dartmouth-Hitchcock Med. Cent., Hanover, NH, USA. Cancer Research (1984), 44(3), 949-54. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 100:131975 AN 1984:131975 CAPLUS

Abstract

A calcitonin (CT) [9007-12-9] producing cell line (DmS53) established from human small cell carcinoma of the lung was grown as 3-dimensional multicellular spheroids in spinner culture or on agar in multiwells, and as tumors in nude (athymic) mice. CT release into the media was directly proportional to spheroid vol. The response of these cells following exposures to x-irradn., adriamycin [23214-92-8], or diazoacetylcholine iodide [89434-93-5] was assessed by monitoring levels of CT released into the media by individual spheroids. Levels of CT in the blood of nude mice bearing DMS53 xenografts were directly proportional to tumor vol. and decreased proportionally with tumor response to x-irradn. and cisplatin [15663-27-1] treatment. Thus, the DMS53 spheroid and xenograft models may be useful systems to monitor responses to therapy utilizing CT as an indicator of tumor burden.

Answer 112:

Bibliographic Information

Chemotherapy of human yolk sac tumor heterotransplanted in nude mice. Sawada, Masumi; Matsui, Yoshiaki; Okudaira, Yoshio. Res. Inst. Microb. Dis., Osaka Univ., Suita, Japan. JNCI, Journal of the National Cancer Institute (1983), 71(6), 1221-5. CODEN: JJIND8 ISSN: 0198-0157. Journal written in English. CAN 100:96258 AN 1984:96258 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The chemotherapeutic effects of cis-diamminedichloroplatinum [15663-27-1] plus vinblastine [865-21-4] plus bleomycin [11056-06-7] (PVB) on 3 human yolk sac tumors (YST-1, YST-2, and YST-3) of the ovary, which were heterotransplanted into BALB/c nude mice, were compared with the effects of vincristine+actinomycin D+cyclophosphamide (VAC), the combination currently favored for treatment of yolk sac tumors. Both PVB and VAC significantly reduced the tumor vol. of all the treated tumors. The mean wts. of tumors in animals treated with PVB or VAC were, in percent of the mean tumor wt. in untreated animals: 1.3 and 1.6 for YST-1, 2.5 and 3.3 for YST-2, and 5.5 and 2.7 for YST-3, resp. A strong correlation was noted between tumor vol. and α-fetoprotein level in the sera of mice bearing YST-1 or TST-2 tumors.

Answer 113:

Bibliographic Information

Chemotherapy and radiation therapy of human medulloblastoma in athymic nude mice. Friedman, Henry S.; Schold, S. Clifford, Jr.; Varia, Mahesh; Bigner, Darell D. Med. Cent., Duke Univ., Durham, NC, USA. Cancer Research (1983), 43(7), 3088-93. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 99:63962 AN 1983:463962 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The human medulloblastoma cell line TE-671 was grown s.c. and intracranially in athymic nude mice. Tumor-bearing animals treated with chemotherapeutic agents or radiation were compared to untreated tumor-bearing controls. Tumors growing s.c. were sensitive to cyclophosphamide [50-18-0] and vincristine [57-22-7] with growth delays in duplicate trials of 15.8/16.5 and 12.9/15.0 days, resp. These tumors were minimally responsive to the 2,5-bis(1-aziridinyl)-3,6-dioxodiethyl ester of 1,4-cyclohexadiene-1,4-dicarbamic acid [57998-68-2] and cis-diamminedichloroplatinum II [15663-27-1] and unresponsive to methotrexate [59-05-2], NSC 351521 [72732-56-0], NSC 409962 [154-93-8], and procarbazine [671-16-9]. Radiation therapy with 2500 or 1500 rads as a single fraction produced a marked response, with growth delays of 39.5 and 21.1 days, resp. Cyclophosphamide produced a significant increase in the median survival of mice with intracranial tumors. Vincristine produced a minimal increase in the median survival while no response was seen to the 2,5-bis(1-aziridinyl)-3,6-dioxodiethyl ester of 1,4-cyclohexadiene-1,4-dicarbamic acid at the dose level and schedule tested. This model system will allow further anal. of the therapeutic sensitivity of human medulloblastoma to other agents or combined-modality regimens.

Answer 114:

Bibliographic Information

NCX-4040, a nitric oxide-releasing aspirin, sensitizes drug-resistant human ovarian xenograft tumors to cisplatin by depletion of cellular thiols. Bratasz Anna; Selvendiran Karuppaiyah; Wasowicz Tomasz; Bobko Andrey; Khramtsov Valery V; Ignarro Louis J; Kuppusamy Periannan Center for Biomedical EPR Spectroscopy and Imaging, Davis Heart and Lung Research Institute, Department of Internal Medicine, The Ohio State University, Columbus, OH 43210, USA. kuppusamy.1@osu.edu Journal of translational medicine (2008), 6 9. Journal code: 101190741. E-ISSN:1479-5876. (COMPARATIVE STUDY); Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, N.I.H., EXTRAMURAL) written in English. PubMed ID 18302761 AN 2008180020 MEDLINE (Copyright (C) 2008 U.S. National

Library of Medicine on SciFinder (R))

Abstract

BACKGROUND: Ovarian carcinoma is the leading cause of mortality among gynecological cancers in the world. The high mortality rate is associated with lack of early diagnosis and development of drug resistance. The antitumor efficacy and mechanism of NCX-4040, a nitric oxide-releasing aspirin derivative, against ovarian cancer is studied. METHODS: NCX-4040, alone or in combination with cisplatin (cis-diamminedichloroplatinum, cDDP), was studied in cisplatin-sensitive (A2780 WT) and cisplatin-resistant (A2780 cDDP) cell lines as well as xenograft tumors grown in nude mice. Electron paramagnetic resonance (EPR) was used for measurements of nitric oxide and redox state. Immunoblotting analysis of A2780 cDDP tumor xenografts from mice was used for mechanistic studies. RESULTS: Cells treated with NCX-4040 (25 microM) showed a significant reduction of cell viability (A2780 WT, 34.9 +/- 8.7%; A2780 cDDP, 41.7 +/- 7.6%; $p < 0.05$). Further, NCX-4040 significantly enhanced the sensitivity of A2780 cDDP cells (cisplatin alone, 80.6 +/- 11.8% versus NCX-4040+cisplatin, 26.4 +/- 7.6%; $p < 0.01$) and xenograft tumors (cisplatin alone, 74.0 +/- 4.4% versus NCX-4040+cisplatin, 56.4 +/- 7.8%; $p < 0.05$), to cisplatin treatment. EPR imaging of tissue redox and thiol measurements showed a 5.5-fold reduction ($p < 0.01$) of glutathione in NCX-4040-treated A2780 cDDP tumors when compared to untreated controls. Immunoblotting analysis of A2780 cDDP tumor xenografts from mice treated with NCX-4040 and cisplatin revealed significant downregulation of pEGFR (Tyr845 and Tyr992) and pSTAT3 (Tyr705 and Ser727) expression. CONCLUSION: The results suggested that NCX-4040 could resensitize drug-resistant ovarian cancer cells to cisplatin possibly by depletion of cellular thiols. Thus NCX-4040 appears to be a potential therapeutic agent for the treatment of human ovarian carcinoma and cisplatin-resistant malignancies.

Answer 115:

Bibliographic Information

Non-cross-resistant sequential combination chemotherapy consisting of cis-diammine-dichloroplatinum (II) mainly, based on synchronization theory, in human bladder cancer xenografts in athymic nude mice.
Yamauchi T; Okada K; Yoshida O Hinyokika kiyo. Acta urologica Japonica (1986), 32(12), 1781-97. Journal code: 0421145. ISSN:0018-1994. (ENGLISH ABSTRACT); Journal; Article; (JOURNAL ARTICLE) written in Japanese. PubMed ID 2435129 AN 87152887 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

We examined the chemotherapies with cis-diamminedichloroplatinum (II) (CDDP) alone and in combination, using the human bladder cancer xenografts (BT-8 and BT-11 strains) in athymic nude mice (BALB/C), to establish the most effective and useful method for urothelial cancer in clinical use. First, to assess the anti-tumor activities of single-drug and our devised VPM or CisCF combination chemotherapies, experiments were done using the BT-8 strain bladder cancer (transitional cell carcinoma and grade III). The schedule and dosage of each chemotherapy were as follows. Vincristine (VCR): 0.06 mg/kg, days 1-6, peplomycin (PEP): 0.9 mg/kg, days 1-6, methotrexate (MTX): 0.6 mg/kg, days 1-6, cytosine arabinoside (Ara-C): 3 mg/kg, days 1-6, 5-fluorouracil (5-FU): 30 mg/kg, days 1-6, adriamycin (ADM): 3 mg/kg, days 1-6, cyclophosphamide (CPM): 10 mg/kg, days 1-10, and CDDP: 2.5 mg/kg, days 1-6. These were for single-drug chemotherapies. The VPM combination consisted of VCR (0.06 mg/kg, days 1 and 4), PEP (0.3 mg/kg, days 1-6) and MTX (0.3 mg/kg, days 2, 3, 5 and 6), and the CisCF combination consisted of CDDP (2.5 mg/kg, days 1 and 4), Ara-C (3 mg/kg, days 1 and 4) and 5-FU (15 mg/kg, days 2, 3, 5 and 6). The control group was given normal saline of 0.1 ml/20 g body weight, intraperitoneally. All anti-cancer drugs were also given intraperitoneally. Secondly, to assess the anti-tumor activities of CDDP alone and various modes of combination chemotherapies with or without CDDP, the following experiments were done using the BT-11 strain bladder cancer (a mixed type of transitional cell carcinoma and squamous cell carcinoma). CDDP: 2.5 mg/kg, days 1-6. VPM X 2: VCR (0.04 mg/kg, days 1, 4, 8 and 11), PEP (0.2 mg/kg, days 1-4) and MTX (0.2 mg/kg, days 2, 3, 5, 6, 9, 10, 12 and 13). CisCF X 2: CDDP (2.5 mg/kg, days 1 and 8), Ara-C (3 mg/kg, days 1, 6, 8 and 13) and 5-FU (30 mg/kg, days 3, 4, 5, 10, 11 and 12).

VPM-CisCF (I): VCR (0.04 mg/kg, days 1 and 4), PEP (0.2 mg/kg, days 1-7), MTX (0.2 mg/kg, days 2, 3, 5 and 6), CDDP (2.5 mg/kg, day 8), Ara-C (3 mg/kg, days 8 and 13), and 5-FU (30 mg/kg, days 10-12).(ABSTRACT TRUNCATED

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Sequential combination chemotherapy consisting of vincristine, peplomycin, methotrexate, cis-diamminedichloroplatinum (II), cytosine arabinoside and 5-fluorouracil, for advanced urothelial cancer. Yamauchi T; Hida S; Ooishi K; Okada K; Yoshida O Hinyokika kiyo. Acta urologica Japonica (1985), 31(7), 1093-104. Journal code: 0421145. ISSN:0018-1994. (CASE REPORTS); (ENGLISH ABSTRACT); Journal; Article; (JOURNAL ARTICLE) written in Japanese. PubMed ID 2414981 AN 86047350 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Two VPM-CisCF chemotherapy regimens (vincristine (VCR), peplomycin (PEP), methotrexate (MTX), cis-diamminedichloroplatinum (II) (CDDP), cytosine arabinoside (Ara-C) and 5-fluorouracil (5-FU), established using human bladder cancer xenografts in nude mice were applied for advanced urothelial cancer. VPM-CisCF (I) consisted of 0.4 mg/m2 VCR on days 1 and 4, 2 mg/m2 PEP on days 1-7, 2 mg/m2 MTX on days 2, 3, 5 and 6, 20 mg/m2 CDDP on days 8, 20 mg/m2 Ara-C on days 8 and 13, and 150 mg/m2 5-FU on days 10-12. VPM-CisCF (II) consisted of 0.6 mg/m2 VCR on days 1 and 3, 3 mg/m2 PEP on days 1-4, 3 mg/m2 MTX on days 2 and 3, 35 mg/m2 CDDP on day 4, 20 mg/m2 Ara-C on days 4 and 7, and 200 mg/m2 5-FU on days 5 and 6. These doses were adjusted for each case: the above mentioned dose x [(80/(40 + Age))2 + (Karnofsky's performance status/100)2]. VPM-CisCF (I) was administered to 6 patients (bladder cancer and transitional cell carcinoma), intra-arterially in two cases. One patient showed a complete response and survived for 7 months, three partial response (PR) surviving for 13, 8 and 37 (arterial-infused case) months, one showed minor response (MR) surviving for 4 months, and one had no change (NC) surviving for 5 months. VPM-CisCF (II) was administered to 11 patients (1 ureteral cancer, 1 renal pelvic cancer, 9 bladder cancer, and 10 transitional cell carcinoma except a case of mixed type of transitional cell carcinoma and squamous cell carcinoma). Four of the patients who had PR survived for 9, 8, 8 and 7 (alive) months, two who had MR survived for 8 and 4 months, three who had NC survived for 6, 4 and 4 months, and who two had progressive disease survived for 8 and 6 months. The major toxicities were myelosuppression and gastrointestinal symptoms, especially nausea and vomiting, but the treatment was well-tolerated.